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ACUTE PANCREATITIS

The Fate of the Patient Surviving One or More Acute Attacks

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IN spite of a great deal of attention that has been devoted to the subject of pancreatitis in recent years, many gaps exist in understanding of this disease. The purpose of this study was to follow the progress of a group of patients who had survived one or more attacks of acute pancreatitis, and thus to help clarify the natural life history of the disease if untreated and evaluate the results of various forms of surgical therapy used.

CRITERIA FOR DIAGNOSIS

For a study of this type, criteria for the diagnosis of acute pancreatitis were essential. This diagnosis was accepted if the patient had a clinical picture compatible with the disease and also either had a serum amylase level of over 60 Russell units per 100 cc.‡ or had fat necrosis and other evidence of acute pancreatitis at operation, or both.

MATERIAL STUDIED

With these criteria the diagnosis of acute pancreatitis could be made in 134 patients in the Massachusetts General Hospital in the years 1946–1951. Of these, 16 died in the acute attack, giving a mortality of 12 per cent. This mortality compares favorably with previous experience at this hospital, the mortality being 18 per cent for the period 1937–1941, 31 per cent for the period 1942–1944 and 12 per cent for the period 1945–1947, according to unpublished data collected by Brignone and Simeone.[1] The apparent improvement after 1945 may reflect the use of antibiotics as well as other advances in diagnosis and treatment.

We have attempted to follow the clinical course of the remaining 118 patients who survived the acute attack of pancreatitis. Some of them had no subsequent treatment, and in others various surgical procedures were performed as definitive treatment of the disease. There was no postoperative mortality.

In age these 118 patients ranged from twenty-seven to eighty-six years, with a distribution by decades as shown in Table 1, the greatest incidence being in the seventh decade. The sexes were almost equally represented, with a slight preponderance of females (54 males and 64 females).

During the same period of years there were 9 cases in which an acute attack closely followed and appeared to have been precipitated by a surgical operation in the region of the pancreas. The attack followed gastrectomy in 6 of these and choledochostomy in 3. These cases have been excluded from this series because it seems probable that direct trauma to the pancreas was the etiologic factor in the acute pancreatitis; they form a special group in which the natural history of the disease may not be comparable to that of the usual form of acute pancreatitis.

TABLE 1. *Age Distribution by Decades.*

AGE yr.	No. OF PATIENTS
21–30	6
31–40	14
41–50	11
51–60	23
61–70	41
71–80	17
81–90	5
Total	117*

*One patient declined to give her age.

In the same period 14 patients were seen in episodes that could not be called acute pancreatitis by the criteria for diagnosis in this study but in which there was definite evidence of chronic pancreatitis. In all these cases the diagnosis of chronic pancreatitis was eventually confirmed by pathological examination. Although many of the patients may have suffered episodes of acute pancreatitis in the early stages of their disease, no such episodes occurred while they were under our observation. These cases have also been excluded from this series,

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‡The upper limit of normal in this laboratory is 40 Russell units.

TABLE 2. *Data in Patients Surviving Acute Attack with No Subsequent Definitive Treatment.*

PATIENT	HOSPITAL NO.	AGE	SEX	NO. OF PREVIOUS ATTACKS	SERUM AMYLASE units/100 cc.	OPERATION DURING ACUTE ATTACK	GRAHAM TEST AFTER ACUTE ATTACK	FOLLOW-UP PERIOD	RESULT	REMARKS
		yr.						mo.		
H. McC.	557484	28	M	<5	118	—	—	63	Good	Patient has chronic nephritis
J. L.	713553	66	F	1	70	—	—	18	Good	Cholecystectomy (1921)
A. L.	715975	75	F	<5	163	—	—	17	Good	Patient has myasthenia gravis; pancreatic lithiasis found on x-ray study.
E. L.	626976	32	M	1	238	Exploratory laparotomy	Normal function	44	Poor	Acute pancreatitis found at operation
M. LaG.	427103	40	F	>5	78	—	—	7	Poor	—
A. K.	530896	65	F	1	20	Cholecystostomy	—	0	?	Acute pancreatitis found at operation; stone in gall bladder.
J. K.	707159	71	F	<5	64	Exploratory laparotomy	—	1	Fair	Acute pancreatitis found at operation; many stones in gall bladder.
W. H.	370057	70	M	0	195	—	Normal function	52	Poor	—
J. H.	603086	46	M	<5	100	—	Poor concentration	14	Fair	Laparotomy 2 yr. previously for acute pancreatitis
E. H.	387805	65	M	0	63	Exploratory laparotomy; incision and drainage of pancreatic abscess.	—	27	Good	No gallstones at operation
A. H.	658719	54	F	0	36	Exploratory laparotomy	—	25	Good	Acute pancreatitis at operation; no gallstones.
R. G.	582150	31	F	0	76	Exploratory laparotomy	—	1	Good	Acute pancreatitis at operation; no gallstones.
S. G.	681479	62	M	>5	197	—	—	18	Good	—
A. Z.	40401	84	F	1	81	—	—	26	Good	Cholecystectomy (1919); patient died after leg amputation.
M. E.	504199	66	F	0	157	—	—	11	Good	—
W. D.	582416	50	M	0	22	Exploratory laparotomy	Normal function	53	Good	Acute pancreatitis found at operation
F. DeN.	717753	63	F	>5	86	—	—	17	Poor	Relief after subsequent cholecystectomy
E. DeL.	275101	55	F	0	94	—	Normal function	39	Good	—
W. C.	712075	28	M	1	158	Exploratory laparotomy	Normal function	22	Poor	Acute pancreatitis found at operation
A. C.	543015	69	M	>5	84	—	Normal function	26	Fair	Patient died of lymphoma; pancreatic lithiasis found on x-ray study.
H. C.	348681	84	F	>5	127	—	—	66	Good	—
L. C.	516994	73	F	?	92	—	—	—	?	—
C. A.	399025	57	F	>5	155	—	—	27	Poor	Previous cholecystectomy (1943)
H. N.	281960	73	M	0	109	—	—	1	Good	—
R. P.	141956	69	F	0	143	—	—	61	Good	Previous cholecystectomy (1931)
C. P.	434157	33	M	0	189	—	—	65	Good	Patient has hypercholesterolemia (cause undetermined)
W. S.	385525	81	M	1	170	—	No filling	33	Good	—
W. S.	519565	65	M	0	93	Exploratory laparotomy	—	36	Good	Acute pancreatitis found at operation
J. S.	620547	72	F	>5	133	—	Normal function	37	Good	—
H. S.	638203	37	M	0	158	—	Normal function	30	Good	—
D. S.	589723	77	M	>5	115	—	Normal function	5	Good	Patient died of cancer of prostate
F. T.	443185	37	M	>5	99	—	Normal function	9	Poor	Pancreatic lithiasis found on x-ray study
A. W.	252620	72	F	0	27	Exploratory laparotomy	—	0	?	Acute pancreatitis found at operation
G. W.	474249	72	F	>5	98	—	Normal function	63	Good	—
R. W.	23945	70	M	>5	93	—	No filling	32	Fair	Previous gastrectomy; patient has stomal ulcer.
E. W.	595505	81	F	0	124	—	—	43	Good	—
W. W.	649059	67	M	1	67	—	No filling	38	Good	—
A. Y.	547808	57	M	>5	54	Cholecystostomy	—	65	Poor	Acute pancreatitis, with normal gall bladder, found at operation
J. H.	366130	41	M	>5	73	—	No filling	54	Good	—
G. S.	516145	36	M	1	88	—	—	68	Good	Previous right colectomy and resection of sigmoid for post-appendectomy fecal fistula
E. C.	103684	60	M	0	71	—	No filling	39	Good	Previous subtotal gastrectomy for duodenal ulcer
F. L.	367430	70	F	0	146	—	—	20	Fair	Cholecystectomy 6 wk. before attack; common duct not explored; patient died of chronic nephritis and uremia.

but the results of therapy are briefly discussed along with those meeting the criteria for diagnosis mentioned above.

Results

No Definitive Treatment

There were 42 patients who had no definitive treatment after recovery from the acute attack. Sixteen had had no previous similar attacks, 12 had had from one to five, and 13 had had over five. There was no information on this point in 1 case.

Five patients had had a cholecystectomy six weeks to twenty-seven years before the acute attack of pancreatitis under study. Nine had an exploratory laparotomy, and 2 a cholecystostomy during the acute attack.

Cholecystography was done after the acute attack had subsided in 17 cases, showing normal gall-bladder filling in 11, poor concentration of dye in 1 and no filling in 5.

Ten of these 42 patients could not be traced or had follow-up periods of less than a year, which was considered inadequate for evaluation. Four patients died of causes unrelated to the gastrointestinal tract during the follow-up period.

Of the 32 patients who were traced for periods varying from twelve to sixty months, 22 had no similar attacks, and these cases are classed as good results. In 4 patients, who had vague upper abdominal complaints, the results were considered fair, and in 6 the symptoms recurred and the results were classified as poor. One of these 6 had a subsequent cholecystectomy at another hospital, with relief of symptoms.

The 13 patients who had had more than five previous attacks are of particular interest because of the possible importance of this factor in prognosis. Six had no further attacks, 2 had vague symptoms, and 5 continued to have similar attacks. The data in this group of cases are presented in Table 2.

Cholecystectomy and Choledochostomy

In 59 cases cholecystectomy and choledochostomy were performed at varying intervals after the onset of the acute attack. As carried out in this hospital, common-duct exploration includes the passage of graduated Bakes dilators into the duodenum.[2, 3] This dilatation is usually carried out up to 6 or 7 millimeters, and sometimes to larger sizes in greatly dilated ducts.

Eight patients could not be traced or had follow-up periods of less than a year. Of the remaining 51, who were followed for twelve to seventy-two months, results were good in 47, fair in 2 and poor in 2. Of the last 2 patients, 1 has had repeated attacks of pancreatitis; the other had three attacks in the first three years after operation but none for the last two years; incidentally, the patency of the ampulla was not established at operation in either of these patients, and the possibility of a residual common-duct stone cannot be excluded.

Of 35 patients who had had more than five previous attacks, 28 were traced for a year or more, results being considered good in all but 2 cases, which were classified as fair.

In most cases an interval of several weeks was allowed to elapse between the acute attack and operation. However, in 12 patients the interval was less than a week, and in 22 it was two weeks or less. These patients had no more postoperative difficulties than those in whom the interval was longer. A review of the records shows that all these patients had two things in common: they were improving clinically, and the serum amylase level was falling at the time the operation was done.

Most of these patients had stones in the gall bladder or common duct or both. Of the 9 who had no stones, 1 was untraced; results were good in 5, fair in 2 and poor in 1.

A cholecystogram was done on 35 patients before operation. Of 26 patients in whom the cholecystogram showed some abnormality in the biliary system, 20 had a good, 1 a fair, and 1 a poor result. Four had been followed for less than a year. Nine patients had normal gall-bladder function by cholecystogram. Of these, results were good in 6 and fair in 1; 2 had inadequate follow-up periods.

The data on these patients treated by cholecystectomy and choledochostomy are presented in detail in Table 3.

Miscellaneous Surgical Procedures

There were 13 patients in this group. Although the number is too small to permit any conclusions to be drawn, it is of some interest that of 9 patients treated by cholecystectomy alone, results were good in 7, fair in 1 and poor in 1 (Table 4).

Choledochostomy (Previous Cholecystectomy)

Four patients who had had a previous cholecystectomy, with continuing attacks of acute pancreatitis, were treated by choledochostomy. One has been traced for less than a year after operation. One patient was without symptoms eighteen months after operation; another had a good result until her death sixteen months after operation from carcinoma of the palate. One traced for thirty-three months has a fair result. The data on these patients appear in Table 5.

Discussion

At first glance the results in the 42 patients who had no definitive treatment after the acute attack seem surprisingly good. However, this group contains a large number of patients (28) who had less than five previous attacks, and of these 16 entered the hospital at the time of the first attack. When compared with the 13 patients who had more than five previous attacks, these 28 did better. Of these

28 patients 6 were followed for less than a year, and the results were classed as good in 17, fair in 2 and poor in 3; of the 13 patients with more than five previous attacks 3 were followed for less than a year; results were good in 5, fair in 2 and poor in 3. absence of biliary disease as shown by cholecystogram does not seem to be of help in prognosis.

The group of 59 patients treated by cholecystectomy and choledochostomy (Table 3) are of particular interest. Although this type of surgical procedure

TABLE 3. *Results after Cholecystectomy and Choledochostomy.*

Patient	Hospital No.	Age	Sex	No. of Previous Attacks	Graham Test	Interval between Onset and Operation	Serum Amylase	Gall-stones	Common-Duct Stones	Follow-up Period	Result	Remarks
		yr.					units/100 cc.			mo.		
M. F.	520470	67	M	1	Negative	24 days	88	Absent	Absent	72	Good	Pancreas much reddened, with thickened head; incision and drainage of pseudocyst 6 wk postoperatively.
M. E.	616671	64	F	>5	Positive	3 mo.	132	Present	Present	24	Good	Previous attack with high serum amylase level
M. E.	381427	58	F	>5	Positive	2 mo.	199	Present	Present	36	Good	Slight thickening throughout pancreas; no fat necrosis.
E. E.	691732	61	F	1		6 mo.		Present	Absent	12	Good	Acute pancreatitis at previous laparotomy
R. D.	25809	59	M	1		2 mo.	65	Present	Present	58	Good	Pancreas thickened throughout; biopsy showed acute pancreatitis.
E. D.	665747	49	M	>5	Positive	21 days		Present	Absent	23	Good	Entire pancreas greatly thickened
H. D.	662851	62	M	>5		14 days	160	Present	Present	35	Good	Pancreas normal; no fat necrosis.
M. DeW.	19654	52	F	>5	Positive	2 mo.	178	Present	Absent	37	Good	Pancreas slightly thickened
A. D.	593400	74	F	>5	Positive	9 days	140	Present	Absent	33	Good	Entire pancreas indurated and woody
S. C.	526557	70	F	1		4 days	14	Present	Absent	71	Good	Fat necrosis present
J. C.	648978	27	F	>5	Positive	16 days	150	Present	Absent	5	Good	Fat necrosis present
M. C.	567395	53	M	>5	Positive	7 days	36	Present	Present	61	Good	Acute pancreatitis at operation
R. C.	712502	49	F	1	Positive	6 wk.	177	Present	Absent	17	Good	Pancreas thickened and edematous
W. B.	618358	64	M	1		5 days	25	Absent	Absent	47	Poor	Biopsy showed acute pancreatitis; patency of ampulla not established.
E. B.	537590	30	F	>5	Negative	3 wk.	155	Present	Absent	43	Good	Pancreas thickened throughout
S. B.	507337	72	M	>5		10 days	193	Present	Absent	25	Good	Pancreas thickened throughout
M. B.	717154	66	F	1		4 days	34	Present	Absent	18	Good	Fat necrosis present
W. B.	647240	47	M	>5	Negative	17 days	138	Absent	Absent	31	Fair	Pancreas thickened
G. B.	381964	59	M	>5	Positive	18 days	61	Present	Absent	49	Good	Pancreas nodular
M. B.	622575	86	F	>5	Positive	4 days	127	Present	Present	2	Good	Pancreas somewhat hard
R. A.	696299	51	M	1	Negative	4 days		Present	Absent	24	Good	Pancreas enlarged and consistent with pancreatitis
M. W.	102749	78	M	<5		6 days	150	Present	Absent	47	Good	Pancreas slightly edematous; patient died of carcinoma of esophagus.
M. C.	582330	67	F	>5		3 days	101	Present	Absent	42	Good	Fat necrosis present
W. F.	246464	64	M	>5		?	33	Present	Absent	12	Good	Entire pancreas firm and nodular; patient killed in railroad accident.
A. D.	94953	75	F	>5	Positive	10 days	116	Present	Absent	3	Good	Pancreas felt normal; patient died of homologous serum jaundice 3 mo. later.
A. C.	521912	75	F	>5		16 days	179	Present	Absent	6	Good	Pancreas enlarged 3 times normal size and nodular
T. A.	640299	65	M	0	Positive	6 wk.	118	Present	Present	37	Good	Pancreas normal; patient died of heart attack.

Thus, in the untreated patients the poorer results seem to correlate roughly with a greater number of preceding attacks. The results in these patients with many previous attacks were quite unsatisfactory when no corrective surgery was attempted. This contrasts sharply with the results in the treated group.

Since cholecystography was performed after the acute attack in less than half these patients, no definite conclusions should be attempted. However, normal gall-bladder function was relatively common in these cases (11 out of 16), and the presence or

does not prevent further attacks of pancreatitis in all cases,[4] failures were relatively few, even in the 35 patients who had had multiple previous attacks. It is impossible to determine how much passage of graduated dilators through the papilla of Vater contributed to a successful outcome. It seems significant that there were only 2 poor results in this entire group and that these were the only cases in which the patency of the lower portion of the common duct was never established.

The success of cholecystectomy and choledochostomy in preventing further attacks of pancreatitis

oes not seem to be influenced by the presence or bsence of gall-bladder function as judged by holecystography.

Certainly, the over-all results in this group of atients are sufficiently good to lend support to the hesis that the primary definitive surgical operation n patients with the recurrent attacks of pancreatitis hould be aimed at the biliary tree.[8-10] It should be oted that although a few of the patients in the ntreated group had calcification in the pancreas hat was visible by x-ray examination, none of this reated group showed this finding. This may indicate that adequate surgery on the biliary tree is ffective when the disease is relatively early.

The postoperative course of 22 patients on whom cholecystectomy and choledochostomy were performed one to fourteen days after the onset of the acute attack presented no detectable difference from that of patients with a longer interval. It must be stressed that even though the interval was short, all these patients were improving clinically and showed falling serum amylase levels at the time of operation.

Although relatively few in number, patients who continue to have recurrent bouts of pancreatitis, with or without what is thought to have been adequate surgery on the biliary tree, present difficult problems. In addition to results classified as poor in this study we have observed the 14 patients previously mentioned who had manifestations of proved chronic pancreatitis. Perhaps the poor results listed in this follow-up study include patients in whom a similar pattern of chronic pancreatitis will eventually develop, as indicated by recurrent

TABLE 3 (*Concluded*).

PATIENT	HOSPITAL NO.	AGE	SEX	NO. OF PREVIOUS ATTACKS	GRAHAM TEST	INTERVAL BETWEEN ONSET AND OPERATION	SERUM AMYLASE	GALL-STONES	COMMON-DUCT STONES	FOLLOW-UP PERIOD	RESULT	REMARKS
		yr.					units/100 cc.			mo.		
M. G.	713505	56	F	>5	Positive	6 wk.	131	Present	Absent	23	Good	Pancreas thickened throughout
J. M.	654026	64	F	>5		13 days	140	Present	Present	37	Good	Pancreas enlarged 3 times normal size and rigid
A. P.	694761	36	F	1	Positive	2 days	187	Present	Absent	16	Good	Pancreas normal
C. M.	613840	69	F	1		24 days	150	Present	Present	51	Good	Pancreas not described
M. C.	312010	55	F	>5	Positive	30 days	44	Present	Present	28	Good	Head of pancreas thickened
O. G.	541872	78	F	>5		11 days	130	Present	Absent	48	Good	Pancreas thickened and nodular; patient died of heart attack.
I. G.	663921	53	F	<5		3 days	117	Present	Absent	39	Good	Pancreas lumpy; no fat necrosis.
J. G.	531887	64	F	>5	Positive	18 days	82	Present	Present	30	Good	Pancreas not described
S. H.	400086	71	M	>5	Positive	14 days	174	Present	Present	65	Good	Extensive inflammatory process involving pancreas
M. H.	515806	64	F	>5	Positive	9 days	83	Absent	Absent	0	?	Hard mass in head of pancreas, with small abscess
O. H.	395358	58	F	>5	Positive	3 mo.	73	Present	Absent	53	Good	Old fat necrosis over surface of pancreas
F. H.	624711	38	M	>5	Positive	1 mo.	162	Present	Absent	32	Good	Pancreas not described
J. I.	582717	72	F	<5	Positive	1 day	140	Present	Present	55	Poor	Pancreas not described; patency of ampulla not established.
S. J.	695874	65	F	>5	Negative	2 mo.	104	Present	Absent	47	Good	Pancreas not described
G. K.	557071	65	M	0		18 days	83	Absent	Absent	18	Good	Pancreas indurated
A. K.	640124	63	F	1	Positive	13 days		Present	Present	46	Good	Retroperitoneal inflammatory mass involving pancreas
L. K.	345885	68	F	1		4 mo.	102	Present	Present	36	Good	Pancreas normal
B. M.	606509	34	M	>5	Negative	3 wk.	79	Present	Absent	58	Good	Pancreas 4 times normal size and indurated
M. M.	598554	51	F	>5		2 mo.	121	Present	Present	49	Good	Pancreas nodular
E. M.	562269	39	F	>5	Positive	10 days	68	Present	Present	25	Good	Pancreas enlarged and indurated
P. M.	557682	57	M	0		14 days	18	Present	Absent	64	Good	Abdominal trauma preceded onset; inflammatory mass involving pancreas.
R. P.	559731	48	M	<5		6 wk.	98	Present	Absent	51	Good	Fat necrosis on surface of pancreas
G. P.	687607	64	F	>5	Positive	2 mo.	127	Absent	Absent	24	Good	Pancreas not described
H. P.	712077	58	M	>5	Negative	9 days	146	Present	Present	1	Good	Pancreas thickened throughout
W. R.	247550	62	M	1		14 days	17	Present	Absent	70	Good	Fat necrosis present
S. R.	364417	62	F	0	Negative	8 days	188	Absent	Absent	41	Good	Pancreatic head stony hard and nodular
A. S.	114828	65	F	0	Positive	19 days	82	Absent	Absent	31	Good	Pancreas hard throughout
C. S.	594937	54	M	<5	Negative	1 mo.		Present	Absent	0	?	Fat necrosis present
I. S.	519120	30	F	>5	Positive	10 days	34	Absent	Absent	18	Fair	Pancreas much indurated
A. V.	500758	71	M	0		1 mo.	163	Present	Absent	24	Good	Fat necrosis present
L. V.	681701	65	F	>5		1 day		Absent	Present	29	Good	Pancreatic head thickened and firm; biopsy showed acute pancreatitis.
A. W.	634132	41	M	>5		5 mo.	124	Present	Absent	7	Good	Acute pancreatitis found at previous laparotomy

pain with calcification, pseudocyst formation, or fibrosis of the pancreas and obstruction of the common bile or pancreatic duct.[9, 11] Sphincterotomy,[12-14] splanchnicectomy,[15-20] vagotomy,[21, 22] celiac ganglionectomy,[17] choledochoduodenostomy,[9, 23] gastrectomy[24] and pancreatic resection[25-28] have all been advocated as effective methods of treatment of such problems. Which, if any, of these procedures will eventually prove to be the best in preventing recurrent pancreatitis cannot be predicted at present.

The results of therapy in the 4 patients who had choledochostomy after an attack of acute pancreatitis had followed a previous cholecystectomy might be expected to be comparable to those in the larger group subjected to cholecystectomy and choledochostomy at one operation. Certainly, the results in the two groups are not obviously conflicting, but the group of 4 is too small to permit any conclusions. However, the first case in Table 5 is of sufficient interest to justify some comment in detail. This patient represents the problem of continued attacks of recurrent acute pancreatitis after apparently adequate surgery on the biliary tree and demonstrates that one must be entirely sure that all abnormalities in the biliary tree have been corrected before resorting to a less direct attack on the disease.

This fifty-nine-year-old woman had had a cholecystectomy and posterior gastroenterostomy performed twenty-eight years previously. Attacks of upper abdominal pain, thought to be due to a common-duct stone, led to a choledochostomy in 1941. No stones were found in a large common duct. Later in the same year a subtotal gastric resection was done for a stomal ulcer. The attacks of upper abdominal pain continued and in 1947 were identified as recurrent bouts of acute pancreatitis, with

TABLE 4. *Patients Surviving the Acute Attack Treated by Miscellaneous Surgical Procedures.*

Patient	Hospital No.	Age	Sex	No. of Previous Attacks	Serum Amylase	Graham Test after Acute Attack	Operation	Gall-stones	Follow-up Period	Result	Remarks
		yr.			units/100 cc.				mo.		
B. W.	599666	66	M	<5	120	No filling	Cholecystectomy	Present	31	Good	Subsequent drainage of pancreatic cyst; patient has diabetes.
H. W.	297645	53	M	0	75	No filling	Cholecystectomy	Present	22	Good	Previous gastrectomy for ulcer; patient died of carcinoma of lung.
A. W.	522237	54	M	>5	150	Good function	Cholecystectomy	Absent	60	Poor	Continued frequent attacks
L. S.	600149	?	F	0	—	—	Cholecystectomy	Absent	48	Good	Fat necrosis
J. L.	462352	61	F	>5	81	Stones; no filling.	Cholecystectomy	Present	19	Fair	Patient has diverticulitis of sigmoid
M. L.	444906	34	F	>5	58	No filling	Cholecystectomy	Absent	22	Good	Previous cholecystostomy for acute pancreatitis
A. H.	584267	63	M	<5	125	No filling	Cholecystectomy	Present	39	Good	Pancreas enlarged 3 times normal size and indurated
M. G.	713264	58	M	1	115	Poor filling	Cholecystectomy	Present	17	Good	Pericholecystic abscess found at operation
C. B.	588561	46	F	1	67	No filling	Cholecystectomy	Present	61	Good	Pancreas thickened throughout
T. R.	686824	37	M	>5	172	Good function	Choledochostomy	Absent	24	Fair	Patient has duodenal ulcer
R. B.	668948	29	M	0	77	—	Choledochostomy	Absent	33	Good	Acute hemorrhagic pancreatitis
M. S.	622705	37	F	>5	21	—	Closure of cholecystduodenostomy; choledochostomy.	Absent	38	Fair	Subsequent small-bowel obstruction
J. R.	714185	47	M	<5	132	—	Cholecystjejunostomy	Absent	18	Poor	Continued attacks; abdominal mass (? pancreatic cyst).

TABLE 5. *Data in Patients with Choledochostomy (Previous Cholecystectomy).*

Patient	Hospital No.	Age	Sex	Interval after Cholecystectomy	No. of Previous Attacks	Interval between Onset and Operation	Serum Amylase	Common-Duct Stones	Follow-up Period	Result	Remarks
		yr.					units/100 cc.				
I. F.	14830	59	F	28 yr.	5	6 wk.	150	Present	18	Good	Pancreas thickened; remnant of gall bladder present.
M. H.	605161	61	F	11 mo.	1	4 wk.	130	Absent	16	Good	Patient died of carcinoma of palate
F. M.	722085	67	F	4 mo.	5	5 wk.	32	Absent	6	Good	Biopsy showed acute pancreatitis
L. M.	124673	48	F	23 yr.	5	11 days	200	Absent	33	Fair	Cystic-duct stump containing stones present

elevated serum amylase and lipase levels. Two years later a bilateral splanchnicectomy was done, with no alteration in the pattern of the attacks. Finally, in 1951, the common duct was re-explored, and a 1.5-cm. stone removed. A remnant of gall bladder that corresponded exactly in size to the stone found in the common duct was found and removed. The patient has subsequently been well and free of attacks.

Summary and Conclusions

Results in a group of 118 patients who survived one or more attacks of acute pancreatitis are presented. Sixteen patients died of acute pancreatitis, a mortality of 12 per cent. Improvement in the mortality as compared with previous experience in this hospital may reflect the use of antibiotics as well as other advances in diagnosis and treatment.

The course of patients who received no definitive treatment after the acute attack was followed in an attempt to clarify the natural history of the disease.

Results in patients treated by various forms of definitive surgical procedures are presented.

Patients in this series who were treated by cholecystectomy and choledochostomy did surprisingly well. The 2 so treated who continued to have serious attacks of pancreatitis were the only patients in whom patency of the ampulla was never established. The suggestion is made that cholecystectomy and choledochostomy may be most effective in patients in whom recurrent attacks of pancreatitis have not produced permanent changes such as calcification in the pancreas.

We urge an alert attitude in the detection of attacks of acute pancreatitis and appropriate surgery on the biliary tree after the acute attack has subsided. This program seems to offer the best approach to the prevention of the serious late manifestations of recurrent pancreatitis that are so difficult to manage.

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CLINICAL STUDIES WITH CARBOMYCIN*

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CARBOMYCIN, a recent addition to the antibiotic family, is produced by *Streptomyces halstedii*.[1] Studies in vitro and in vivo have shown that the substance is active against gram-positive bacteria but has little or no effect on most pathogenic gram-negative micro-organisms.[1-3] Early reports indicate that this antibiotic is effective against some gram-positive bacteria that have become resistant to other antibiotics.[2-4] Carbomycin is primarily a bacteriostatic agent.[2]

This report describes our experience in the treatment of 30 patients with bacterial infections caused by beta-hemolytic streptococci, coagulase-positive *Staphylococcus aureus*, pneumococci and *Neisseria gonorrhoae*.

Methods and Materials

All patients were young men between eighteen and thirty-two years of age in good physical condition. Twenty-three with streptococcal infections were admitted to the hospital six to thirty-six hours after the initial symptoms had begun. Nineteen of these patients had exudative tonsillitis, 3 had acute pharyngitis, and 1 had scarlet fever. White-cell and differential counts, urinalysis and throat culture were performed on admission before treatment. The throat cultures were grown on plates containing Difco's blood-agar base with 5 per cent human blood added. Throat cultures were repeated in forty-eight hours in all but 1 case and again in ninety-six hours and at the end of seven days in most patients. The urinalysis and white-cell and differential counts were repeated on the seventh day. A heterophil-antibody titer was obtained in all patients who were not afebrile in seventy-two hours. Several dosage schedules were employed to determine the most satisfactory regimen (Table 1). The carbomycin was usually given with milk. No aspirin or gargles were administered.

Patients with tonsillitis or pharyngitis who were included in this series met the following criteria: history of a sore throat with a sudden febrile onset; moderate to excessive amount of white exudate on the tonsils or pharynx (21 patients) — 2 patients (Cases 20 and 22) had no exudate but showed marked reddening of the pharynx; tender cervical lymphadenopathy; and beta-hemolytic streptococci on the pretreatment throat culture. In all but 2 cases the white-cell counts were 10,500 or above, ranging from 8250 to 30,000 and averaging 17,350. Cases 14 and 15, who had white-cell counts of 8250 (with 89 per cent neutrophils) and 9500 (with 71 per cent neutrophils) respectively, are included because they fulfill the basic criteria.

One patient (Case 24) had an exudative tonsillitis. The initial throat culture showed a heavy growth of coagulase-positive *Staph. aureus* and no streptococci. He was given 500 mg. of carbomycin every six hours for twenty-seven doses.

Another patient experienced a sudden onset of chills, fever, cough and rusty sputum. A chest film showed massive involvement of the left upper lobe, and a sputum culture demonstrated numerous pneumococci. This patient was given carbomycin, 300 mg. every six hours for twenty doses, followed by 200 mg. every six hours for twelve doses.

Five patients with acute urethritis due to *N. gonorrhoae* were treated as outpatients. They were given 500 mg. of carbomycin every six hours for two or three days (Table 2). The following criteria were present in all 5 patients: sexual contact within twenty days of the onset of symptoms; purulent urethral discharge; and a smear of the urethral discharge showing many gram-negative intracellular and extracellular diplococci.

Bacterial sensitivities were determined by the usual twofold serial tube dilution method, using Difco's Bacto beef-heart infusion broth, on the organisms isolated from the throats of 7 patients with sore throats caused by beta-hemolytic streptococci (Table 3).

Results

Streptococcal Infections

Carbomycin eliminated beta-hemolytic streptococci from the throat cultures in 18 of 22 patients within forty-eight hours (Table 1). Of the 4 patients with throat cultures showing beta-hemolytic streptococci at forty-eight hours, 2 (Cases 9 and 21) had a normal throat flora at ninety-six hours, and 2 (Cases 1 and 22) continued to show beta-hemolytic streptococci at ninety-six hours; these 2 patients had a normal throat flora at seven days. One patient (Case 18) showed no hemolytic streptococci at forty-eight hours but had a slight growth at ninety-six hours; no streptococci were seen on the throat culture obtained on the seventh day.

In the group of 23 patients with streptococcal infections there were 2 failures and 1 clinical re-

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¶Kindly supplied by Charles Pfizer and Co., Incorporated, Brooklyn, New York. This drug is manufactured under the trade name of Magnamycin.

lapse. Case 12 continued to run a temperature of 101 to 102°F., although the tonsillar exudate disappeared in forty-eight hours and the throat culture failed to show beta-hemolytic streptococci at forty-eight and ninety-six hours. However, because the fever persisted after 8.5 gm. of carbomycin had been given over a period of four and a quarter days, penicillin therapy was administered. The patient became afebrile twenty-four hours later. The heterophil-antibody titer was 1:7.

Case 15 is also classified as a failure. This patient showed a good response in eighteen hours but continued to run a temperature of 99 to 99.4°F. for six and a half days. The exudate on the tonsils disappeared seventy-two hours after therapy with carbomycin. The throat culture, which was negative for beta-hemolytic streptococci at forty-eight hours, showed those organisms at ninety-six hours. Oxytetracycline therapy was started, and twenty-four hours later the patient was afebrile. The heterophil-antibody titer was 1:14.

Case 7 is considered a relapse. This patient responded to treatment in thirty-six hours but experienced a rebound of temperature to 99°F. for an additional twenty-four hours. The throat cultures were negative for beta-hemolytic streptococci at forty-eight, ninety-six and a hundred and twenty hours. He was entirely asymptomatic when he was discharged from the hospital after receiving 7.5 gm. of carbomycin. However, four days later, or nine days after his first admission, he was readmitted to the hospital with severe exudative tonsillitis. Repeated throat cultures showed only nonhemolytic streptococci and *N. catarrhalis*. He responded favor-

TABLE 1. *Patients Treated with Carbomycin for Infections Due to Beta-Hemolytic Streptococci.*

Case No.	Dosage	No. of Doses	Total Dosage	Interval between Treatment and Favorable Response*	Effect on Fever	Culture for Beta-Hemolytic Streptococci			
						Before therapy	After 48 hr.	After 96 hr.	After 7 days
	mg./6 hr.		gm.	hr.					
Patients with exudative tonsillitis:									
1	200	20	4.0	36	No further fever	Positive	Positive	Positive	Negative
2	300	19	5.7	36	No further fever	Positive	Negative		
3	300 200	3 8	4.1	30	No further fever	Positive	Negative		
4	300 200	9 8	4.3	36	Temperature of 100°F. for 68 hr.	Positive	Negative	Negative	
5	300 400	11 8	6.5	78	No further fever	Positive	Negative		
6	500	12	6.0	18	No further fever	Positive	Negative		
7†	500	15	7.5	36	Rebound to 99°F. for additional 24 hr.	Positive	Negative	Negative	Negative (5 days)
8	500	20	10.0	18	No further fever	Positive	Negative	Negative	
9	500	22	11.0	18	No further fever	Positive	Positive	Negative	Negative
10	500	23	11.5	36	No further fever	Positive	Negative	Negative	Negative
11	500	28	14.0	36	Rebound to 99.8°F. for additional 46 hr.	Positive	—	Negative	Negative
12‡	500	17	8.5	(No response)		Positive	Negative	Negative	
13	500	20	10.0	18	No further fever	Positive	Negative	Negative	Negative
14	500	23	11.5	36	No further fever	Positive	Negative	Negative	Negative
15‡	500	23	11.5	18	Rebound to 99.4°F. for additional 160 hr.	Positive	Negative	Positive	
16	500	15	7.5	18	No further fever	Positive	Negative		
17	500	23	11.5	18	Temperature of 99.8°F. for additional 44 hr.	Positive	Negative		
18	500	37	18.5	48	Temperature of 99.2°F. for additional 60 hr.	Positive	Negative	Positive	Negative
19	500	29	14.5	36	No further fever	Positive	Negative	Negative	Negative
Patients with pharyngitis:									
20	300	6							
	200	12	4.2	36	No further fever	Positive	Negative	Negative	
21	300 400	9 8	5.9	24	Temperature of 99.8°F. for additional 46 hr.	Positive	Positive	Negative	
22	500	27	13.5	36	Temperature of 99.2°F. for additional 24 hr.	Positive	Positive	Positive	Negative
Patient with scarlet fever:									
23	300	27	10.1	12	Rebound to 99.8°F. for additional 54 hr.	Positive	Negative		Negative
	400	5							

*A favorable response was judged to be a drop in temperature of at least 3°F. or to a level below 100°F. in association with a decrease in toxic symptoms and improvement of the sore throat. Some patients continued to run a low-grade temperature of 99.2 to 100°F. or experienced a rebound of fever ranging from 99.2 to 99.8°F. after being afebrile.

†Relapse 4 days after treatment was stopped.

‡Failure of treatment.

ably to penicillin in thirty-six hours although an additional eight days were needed before the throat became normal. This case is regarded as a relapse despite the failure to isolate beta-hemolytic streptococci during the second admission. It is possible that carbomycin altered the cultural characteristics of the streptococcus.

Carbomycin may cause a favorable clinical response in eighteen to seventy-eight hours (Table 1). Seven patients, however (excluding the 2 cases regarded as failures and the 1 recurrence), had a rebound of fever (temperatures of 99 to 100°F.) lasting from twenty-four to sixty-eight additional hours.

TABLE 2. *Effect of Carbomycin on Acute Urethritis Due to* N. Gonorrhoeae.

Case No.	Carbomycin Dosage mg./6 hr.	No. of Doses	Total Dosage gm.	Duration of Treatment days	Result
26	500	8	4	2	Failure
27	500	8	4	2	Failure
28	500	12	6	3	Failure
29	500	12	6	3	Failure
30	500	12	6	3	Failure

TABLE 3. *Sensitivity of Various Beta-Hemolytic Streptococci to Carbomycin.*

Case No.	Inhibiting Concentration* micrograms/cc.
1	0.2
4	0.03
5	0.6
9	0.2
14	1.6
20	0.04
23	1.25

*Fractions have been rounded.

Exudative Tonsillitis due to Coagulase-Positive Staph. aureus

The patient with exudative tonsillitis due to coagulase-positive *Staph. aureus* became afebrile in twenty-four hours. Throat cultures were negative for *Staph. aureus* at forty-eight and ninety-six hours. The clinical response was very satisfactory.

Lobar Pneumonia due to Pneumococci

One patient with lobar pneumonia due to pneumococci was treated with carbomycin. This patient had massive involvement of his left upper lobe. The temperature dropped from 104 to 98.6°F. in eighteen hours and remained normal thereafter. A chest film showed 90 per cent resolution in seven days.

Acute Urethritis due to N. gonorrhoeae

Five patients with gonorrhea were treated with carbomycin (Table 2). Two were given 500 mg. every six hours for two days (total dosage of 4 gm.), and 3 were treated with 500 mg. every six hours for three days (total dosage of 6 gm.). Although there was an initial decrease in the urethral discharge in 4 of the 5 patients within twenty-four hours, the discharge again became profuse in forty-eight hours. Urethral smears continued to show gram-negative intracellular and extracellular diplococci at twenty-four and forty-eight hours in all cases and were still positive at seventy-two hours in the 3 patients treated for three days.

Toxicity

Four patients had four or five loose stools daily while taking the antibiotic. One also had nausea for a day. The other patients showed no symptoms attributable to carbomycin.

There was no evidence of suppression of the granulocytic series as manifested by follow-up white-cell and differential counts during the period of observation in any of the hospitalized patients. No albuminuria or abnormal microscopical elements in the urinary sediment were noticed.

Discussion

It appears from this and other studies that carbomycin may be used effectively in the treatment of some infections caused by gram-positive bacteria. Our experience in the treatment of patients with streptococcal infections indicates that 500 mg. every six hours is more satisfactory than smaller doses. Our patients were treated for four to nine days. However, recent reports suggest that regardless of the antibiotic used, treatment for streptococcal sore throats should be continued for ten days as a measure to prevent rheumatic fever.[5] It is therefore likely that the ten-day treatment of streptococcal infections should be employed routinely.

Our data indicate that a favorable response may be expected to occur between eighteen and forty-eight hours after the start of therapy. Seven patients (in addition to the 2 cases considered failures and 1 recurrence), however, manifested a rebound of a low-grade fever, with temperatures ranging from 99 to 100°F., that persisted for twenty-four to sixty-eight additional hours even though the patients' throats showed improvement and the sore throat and systemic symptoms abated. The average clinical response to carbomycin in streptococcal sore throat, therefore, is considerably less rapid than that to penicillin. This is in keeping with the observation that carbomycin is a bacteriostatic agent.

Because carbomycin shows activity against the same general bacterial spectrum as penicillin, and because studies in vitro have indicated activity

against *N. gonorrhoeae*, it was hoped that the antibiotic would be effective in the treatment of gonorrhea. However, our experience with 5 patients discouraged us from trying the medication further in this disease. Not one of the 5 was cured of the condition; 4 showed a temporary lessening in urethral discharge within twenty-four hours, but the discharge again became profuse in forty-eight hours. The smears of the urethral discharge remained positive for *N. gonorrhoeae* in all cases during the period of treatment.

It is evident that carbomycin does not replace any of the better established antibiotics.[7, 8] The future use of the antibiotic seems to be limited to the treatment of conditions caused by gram-positive bacteria that have become resistant to penicillin and the broad-spectrum antibiotics or in significant allergic responses from these drugs. However, as pointed out by Finland et al.,[7] this offers little or no scope.

Summary

Carbomycin was given to 23 patients with infections due to beta-hemolytic streptococci. Throat cultures from 18 of 22 patients were negative for these organisms in forty-eight hours. Of the 23 cases 2 were regarded as failures and 1 as a clinical relapse.

In general a favorable response to carbomycin therapy in streptococcal sore throat occurred within eighteen to forty-eight hours, although a significant number of patients manifested a rebound of a low-grade fever for an additional twenty-four to sixty-eight hours. The average clinical response appears to be considerably less rapid than that to penicillin.

One patient with lobar pneumonia due to pneumococci and 1 with exudative tonsillitis caused by pathogenic *Staphylococcus aureus* responded well to carbomycin.

In the dosage schedules used carbomycin failed to cure 5 patients suffering from gonorrhea.

Carbomycin caused mild diarrhea in 4 of 30 patients. One of these was also slightly nauseated. In general carbomycin, given with milk, was tolerated very well. No toxic effect except the mild gastrointestinal symptoms occurred.

Carbomycin does not appear to replace any of the more established antibiotics in the treatment of diseases caused by beta-hemolytic streptococci.

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THE SIGNIFICANCE OF ASCHOFF BODIES IN THE LEFT ATRIAL APPENDAGE*

A Comparison of 40 Biopsies Removed during Mitral Commissurotomy with Autopsy Material from 40 Patients Dying with Fulminating Rheumatic Fever

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THE development of a practical operation for mitral stenosis during the past five years has provided an unusual opportunity for interval study of the myocardium in a large number of patients with chronic rheumatic heart disease. The high incidence of Aschoff bodies in the surgical specimens has been an unexpected finding (Table 1). In our series of 40 cases it was 55 per cent.

This is out of line with the clinical evidence of rheumatic activity and is especially puzzling since less than half the group had a history of rheumatic fever, and all had been carefully scrutinized to exclude such a diagnosis within the recent past. This discrepancy between the clinical features and the histologic findings is fortunate for the patient but difficult to explain.

In this connection there are two important considerations. In the first place, Is the histopathology of the biopsy specimen fully representative of the ventricular myocardium? There is no evidence to

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the contrary, but on the other hand this special segment of the heart has not heretofore been examined in routine autopsies as carefully as those now available for study. Secondly, Are the current findings analogous to those in patients who actually die with severe rheumatic fever? With these questions in mind we reviewed the unique autopsy material from 40 patients who died at the House of the Good Samaritan during the past twenty-five years with severe fulminating rheumatic fever. Fortunately, these hearts had been preserved intact, and we were able to section the atrial appendages and correlate them with the histologic findings elsewhere in the heart and with the clinical manifestations of the disease.

TABLE 1. *Incidence of Aschoff Lesions in Surgical Specimens.*

AUTHOR	DATE	TOTAL CASES	CASES WITH ASCHOFF BODIES
Pinninger[1]	1951	15	10 (67%)
Kuschner et al.[2]	1952	11	4 (36%)
Sabiston and Follis[3]	1952	43	32 (74%)
Börck et al.[4]	1952	18	8 (44%)
Janton et al.[5]	1952	88	14 (16%)
Entickna p[6]	1953	71	29 (41%)
Decker et al.[7]	1953	183	83 (45%)
Present series	1953	40	22 (55%)
Totals		469	202 (43%)

DATA IN FATAL FULMINATING RHEUMATIC FEVER

Significant murmurs and congestive heart failure were present in all cases. Fever and elevation of the sedimentation rate were almost universal. Other clinical evidence of severe rheumatic fever, including arthritis, pericarditis and nodules, is listed in Table 2. Eleven patients had auricular fibrillation, which was transient in 4 and persistent in 7.

The most striking pathological changes in the atrial appendages were in the endocardium. All were abnormal. Twenty-nine (72 per cent) of the 40 patients showed one or more Aschoff lesions, usually found in the subendocardial region and identical with those seen in the surgical material (Fig. 1). Thirty-eight cases (95 per cent) showed some degree of infiltration with lymphocytes and monocytes. In 23 (58 per cent) this feature was quite prominent.

TABLE 2. *Clinical Findings in Fulminating Fatal Rheumatic Fever.*

CASE NO.	AGE	SEX	INTERVAL SINCE INITIAL ATTACK	NO. OF ATTACKS	MANIFESTATIONS
	yr.				
1*	8	F	18 mo.	1	Nodules
2*	43	F	?	2	Arthritis; rheumatic heart disease with mitral stenosis; no previous history.
3*	6	F	19 mo.	2	Severe heart failure
4*	11	M	7 yr.	4	Pericarditis
5*	10	F	3 yr.	2	Pericarditis, 3 days before death
6*	12	M	5 yr.	2	Nodule; pleurisy terminally.
7*	15	F	6 yr.	5	Arthritis; many nodules; pericarditis.
8*	15	F	2 yr.	2	Patient died 9 hr. after admission in congestive heart failure
9*	8	M	7 mo.	1	Pericarditis; 1 nodule.
10*	17	F	4 yr.	5	Arthritis; many nodules; PR interval 0.20 second.
11*	12	M	2 yr.	1	Pericarditis; arthritis; many nodules; PR interval 0.28 second; erythema marginata.
12*	5	M	1 yr.	1	Arthritis; 1 nodule; epistaxis.
13*	9	F	6 yr.	4	Many nodules; PR interval 0.22 second.
14*	7	M	6 mo.	1	PR interval 0.21 second
15*	6	M	18 mo.	2	Many nodules
16*	8	M	13 mo.	1	One nodule; PR interval 0.22 second.
17*	21	F	10 yr.	3	Low-grade active rheumatic fever with heart failure
18*	10	M	2 yr.	1	Pericarditis; PR interval 0.28 second.
19*	16	F	5 yr.	3	Arthritis
20*	14	M	2 yr.	3	Not at House of Good Samaritan during final illness
21*	11	F	1 yr.	1	Pericarditis; many nodules.
22*	16	F	3½ yr.	1	Chorea; many nodules; pericarditis.
23*	11	F	10 mo.	1	Erythema marginata
24*	9	M	4 mo.	1	Pericarditis; many nodules.
25*	37	F	?	?	Arthritis
26*	9	F	4 yr.	2	Few nodules; PR interval 0.20 second.
27*	15	F	2 yr.	1	Fever and failure
28*	15	M	1 yr.	1 or 2	Pericarditis; arthritis; many nodules; erythema marginata; PR interval 0.21 second.
29*	24	F	5 yr.	3	Pericarditis; pleuritis.
30	15	F	9 yr.	3	Arthritis
31	7	M	2½ yr.	2	Pericarditis; few nodules; PR interval 0.20 second.
32	6	M	18 mo.	1	Pericarditis; arthritis; many nodules.
33	5	M	8 mo.	1	One nodule
34	10	F	3 yr.	2	Pericarditis; PR interval 0.20 second.
35	3	F	8 mo.	1	Epistaxis
36	11	M	9 mo.	2	Pericarditis; pleuritis; PR interval 0.23 second.
37	11	F	9 mo.	2	Pericarditis
38	17	M	2 yr.	2	Occasional fever
39	32	F	?	?	Heart failure; occasional fever; increased corrected sedimentation rate.
40	9	M	3 yr.	1	Few nodules
Averages	13		2.8 yr.		

*Cases showing Aschoff bodies in the atrial appendage.

Nine patients (23 per cent) demonstrated some infiltration with neutrophils and eosinophils. Thirty-eight (95 per cent) had irregular fibrous thickening, which was marked in 24 (60 per cent).

The changes in the myocardium were less prominent. Only 2 patients had definite Aschoff lesions in this location. Thirty-seven cases (93 per cent) revealed some degree of lymphocytic and monocytic

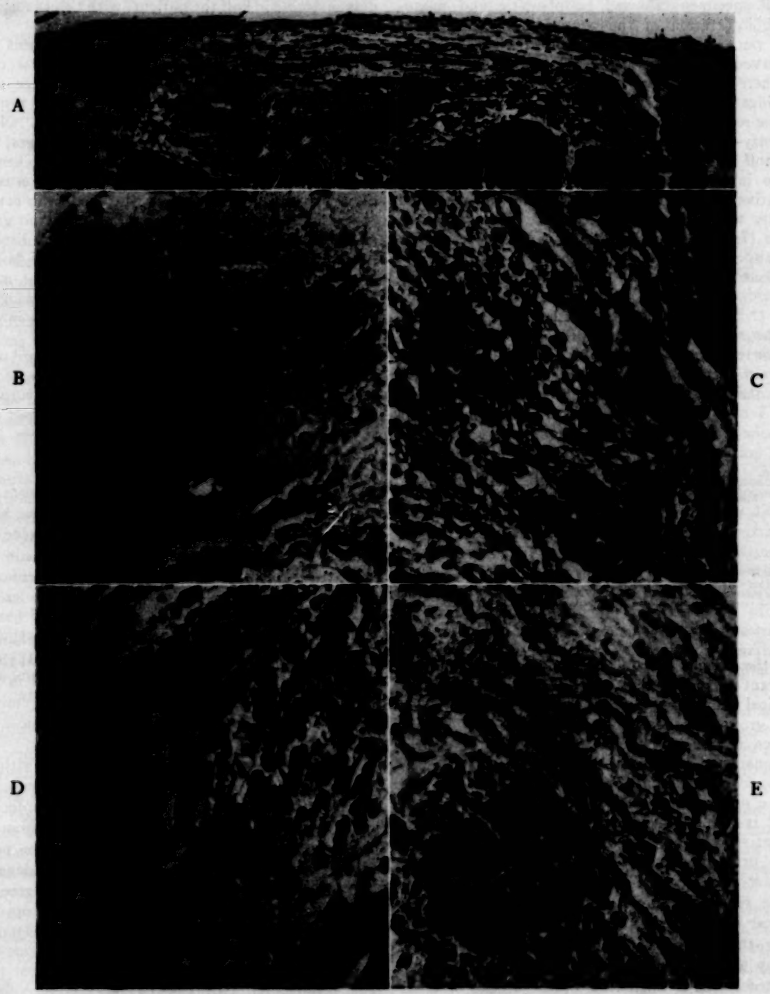

FIGURE 1. *Subendocardial Aschoff Bodies in the Atrial Appendages.*
A, B and C = surgical biopsies obtained at commissurotomy. D and E = autopsy specimens from patients dying with acute rheumatic fever. The lesions are indistinguishable.

infiltration; seven (18 per cent) demonstrated a few scattered neutrophils.

All specimens showed lymphocytic and monocytic infiltration of the pericardium. In 7 cases (18 per cent) acute fibrinous pericarditis was observed.

There was close correlation between the positive findings in the atrial appendages and those noted in the routine sections taken elsewhere in the heart. Twenty-five (85 per cent) of the 29 patients with Aschoff lesions in the atrial appendages also had them in the routine autopsy sections. However, negative findings in the atrial appendage correlated poorly with the general sections. Eight of the 11 cases (73 per cent) disclosing no Aschoff lesions in the appendage did show them in the routine autopsy sections.

Discussion

The striking morphologic identity of the lesions in the two series in spite of the age discrepancy (second decade for the autopsy series as compared with third to fourth decade for the surgical series) and the absence of clinical clues in the older group warrant further critical appraisal. From the pathological standpoint the only difference between the two groups was the higher incidence of Aschoff bodies in the autopsy material. This is clearly demonstrated in Figure 1 and Table 3.

Table 3. *Findings in Atrial Appendages.*

Finding	40 Cases of Fulminating Fatal Rheumatic Fever		40 Surgical Biopsies	
	Endocardium	Myocardium	Endocardium	Myocardium
	%	%	%	%
Aschoff bodies	72	5	55	5
Lymphocytic & monocytic infiltration	95	93	98	90

Supporting evidence of a latent rheumatic state in the surgical series (suggested by the biopsy findings) is becoming evident in the immediate postoperative course of a significant number of patients. The protracted convalescence noted in many, characterized by the delayed appearance of low-grade fever and tachycardia, the persistence for several weeks of pericardial and pleural rubs long after the effects of trauma ordinarily subside, spotty areas of pneumonitis, the frequent appearance of auricular fibrillation on the second or third day, atypical pleuritic chest pain appearing weeks to months postoperatively and, occasionally, acute arthritis all suggest in subtle fashion mild and often unrecognized rheumatic activity. Such a course has characterized approximately 25 per cent of patients in our series and an equal percentage of those in the Philadelphia series of Glover and his associates.[3] In our experience, Aschoff lesions were demonstrable in half the patients with this suspicious postoperative course.

As further controls, we studied the atrial appendage from two other groups. The first consisted of 9 persons over fifty years of age who showed at autopsy severe valvular disease typical of inactive healed rheumatic endocarditis. None of these had Aschoff lesions in the appendages, but most of them did reveal dense fibrous thickening of the endocardium. The second group consisted of 50 persons of various ages who died from causes other than rheumatic fever and who had no gross anatomic evidence of rheumatic heart disease. None of these cases demonstrated Aschoff bodies or any other lesions in the endocardium or myocardium of the appendages. The only pathological changes noted were scattered lymphocytes in the epicardium in a few cases.

Our pathological findings are not in accord with Enticknap's[2] statement that the significance of the lesions resembling Aschoff bodies in the surgical specimens must be questioned because of their distribution and other subtle histologic variations.

Summary and Conclusions

Aschoff lesions are manifestations of tissue reaction to injury, and convincing evidence has been presented over the years that they are specific for rheumatic fever. The incidence of the lesions in the left atrial appendage in fatal cases of rheumatic fever correlates closely with that of similar lesions elsewhere in the heart.

The Aschoff lesions and other histologic changes in the atrial appendage of patients with fatal rheumatic fever are identical with those found in the surgical specimens from patients with mitral stenosis who show no recognizable clinical or laboratory signs of recent rheumatic activity.

No similar lesions were found in patients without rheumatic fever or in 9 patients with rheumatic heart disease who survived beyond the fifth decade and whose hearts were available for comparison.

The conclusion seems inescapable that the presence of Aschoff lesions in the atrial appendage of the surgical specimens indicates some degree of rheumatic activity. Recent observations on the events during the postoperative phase lend clinical support to this concept.

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MEDICAL PROGRESS

FOOD POISONING

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SAN FRANCISCO

IN the broadest sense, food poisoning includes all illnesses arising from the ingestion of food, — food contaminated with pathogenic bacteria or their products, with nematodes or fungi, with chemical poisons and with poisonous plants and food poisonous in itself, — illnesses with a complete range of symptoms and of a great variety of causes. Various groups for various reasons choose to limit the definition according to their interests and preferences. The term is limited by some to acute gastroenteritis caused by ingestion of food or drink containing either bacteria capable of initiating an acute inflammatory reaction of the alimentary tract or toxic substances produced by bacteria that provoke, directly or indirectly, nausea and diarrhea. According to others the term should not include botulism, which only occasionally presents the symptoms of gastroenteritis but is nevertheless a distinctly food-borne disease caused by absorption, from various portions of the intestinal canal, of a specific toxin elaborated by four types of *Clostridium botulinum* or *parabotulinum* under suitable conditions. Some wish to exclude the paralytic poisonings that follow ingestion of certain fish or shellfish. These intoxications are distinct clinical entities in which disturbances of the central nervous system overshadow those of the gastrointestinal tract. Some authors adhere to the deeply entrenched term "food poisoning," common and vague in the medical literature, because it refers to the vehicle of the causative agent. The emphasis on clinical syndromes or on vehicles in the classification, important though they are in fact, obviously diverts attention from the relevant issue — the cause. The reviewer looking at this bulky subject through a veil of inadequate diagnosis and reporting, can only attempt to discuss the food-borne conditions that seem to be the most prevalent and that are receiving the necessary critical attention of physicians, bacteriologists, biochemists and epidemiologists.

The confusion in most cf the literature is reflected in the reporting of the National Office of Vital Statistics, United States Public Health Service, which issues summary tables compiled annually by the Milk and Food Branch of the Division of Sanitary Engineering. Under the title "Food-borne Outbreaks Other than Milk and Milk Products," it lists the reported number of outbreaks and cases diagnosed as botulism, chemical food poisoning, dysentery, food infections, food poisoning, typhoid fever and salmonellosis. The column headed "Miscellaneous and Unknown" in some years covers up to 7 per cent of the total outbreaks reported. A glance at the table for 1948 discloses the disconcerting and confused terminology. Under the heading "Food Infection Bacteriologically Proven," staphylococcal, salmonella and streptococcal infections are listed. Buried in the column headed "Food Poisoning," mostly attributed to staphylococcal enterotoxins, is a single outbreak of mussel poisoning, listed as "Food Poisoning (*Gonyaulax catenella*)." Apparently, the grouping under "Food Poisoning" proved unsatisfactory because later another, "Gastroenteritis," was added. Even the term "Diarrhea," a symptom, has appeared in the tables. "Trichinosis" is a master group listing.

This confusion in reporting the commoner acute gastroenteritides and other food-borne diseases is largely due to vagueness in diagnosis, usually carelessly resting on a vague nondifferential group of symptoms and, with a few exceptions, not on etiology. In consequence it is difficult to know the causes for the apparently increasing incidence of bacterial gastrointestinal disease and to plan concerted public-health efforts to reduce the illness and distress that they cause all over the world.

Feig[1] suggested that the term "food poisoning" be abandoned and that the term "gastroenteritis," modified by the etiologic agent, replace it. This suggestion has in part been followed in the 1950 edition of *The Control of Communicable Diseases in Man*, an official report of the American Public Health Association,[2] in which the term "food poisoning" is now limited to bacterial intoxications attributable to staphylococci and to *Cl. botulinum*. Infectious food poisoning is now treated under headings such as "bacillary dysentery (shigellosis)" and "salmonel-

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losis." This is a step in the right direction because the true nature of the gastroenteritides and other food-borne illnesses can be identified only through critical examination of the epidemiology and particularly of the bacteriology of each outbreak. Unwarranted assumptions that an organism in a given food or in the intestinal tract is the cause of the outbreak should not be accepted. It would be advantageous in the future if outbreaks were listed primarily on the basis of the cause — botulism, fish poisoning, shellfish poisoning, gastroenteritis, as the case may be. When the responsible organism is definitely known, the appropriate modifier — staphylococcal enterotoxin, salmonella, streptococcus or whatever — should be used. The present tendency is to include shigella dysentery with shigellosis. Outbreaks listed with the qualification "probably" salmonella or staphylococcus should be considered gastroenteritis, etiology undetermined. Difficulties will arise when toxic infections with *Escherichia coli, Cl. perfringens (welchii)* or *Bacillus cereus* must be classified.

The usual chemical food poisoning is an illness arising when inorganic compounds are unintentionally introduced, mainly during manufacture or deliberately added to food as preservatives. Proper enforcement of effective food and drug laws and regulations regarding adulteration and preservation has been greatly reduced. The textbooks by Dewberry[3] and by Tanner and Tanner[4] cover this subject thoroughly, and it is not taken up in this review.

Attention has again been called to the difficulties that arise when carbon monoxide poisoning is mistaken for food poisoning.[5] The symptoms are frequently quite similar, except that as a rule diarrhea does not accompany carbon monoxide poisoning. An alert epidemiologist learns that those affected have not shared food, but that they frequent a common location. He knows that carbon monoxide poisoning usually occurs during cold weather. The suspicions are confirmed by determination of the concentration of carbon monoxide in the patients' blood.

From the standpoint of the patient and the attending physician, food poisoning is suspected when several people who partook of a common meal have either acute gastroenteritis or involvement of the central nervous system with subordinate intestinal disturbance. The general practitioner called to treat the patient is in a pivotal position to initiate the steps required to determine the cause or causes of this illness. He observes the early clinical manifestations, and he can direct collection of the specimens essential for specific diagnosis. In only 16 states is he obligated to report his observations to a state health agency. A plea is made here that state health departments be notified by the physician whenever he encounters an outbreak of food poisoning. Too often the responsible investigative agency has to depend on newspaper or radio reports, far too late for a searching epidemiologic investigation. Much of the urgently needed evidence has been consumed, destroyed or disposed of by the time the investigation is undertaken. A short interval between the onset of the illness and report of the cases and a thorough investigation of the cause contribute greatly to the completeness of the records. Only through knowledge of the cause can prevention be planned on a sound basis. Despite the best possible diagnostic efforts many outbreaks, in individual cases, remain unexplained.

One reason that the notification of "food poisoning" has been incomplete is that the physician dealing with the outbreak has had the impression that the health agency — local or state — could render no service to the patient or to the community. With increased interest in effective control measures and with the present availability of personnel fully trained to investigate these illnesses, the physician and the patient may now both benefit from a correct diagnosis. Clinical observations must be supplemented by epidemiologic and laboratory evidence if patients with gastroenteritis are to be treated intelligently. Experience has taught that thorough investigation of one episode frequently unmasks

TABLE 1. *Food-Borne Outbreaks in California, 1943-1952.*

YEAR	TOTAL OUTBREAKS	TOTAL CASES	FOOD POISONING DUE TO STAPHYLOCOCCI		FOOD POISONING DUE TO STREPTOCOCCI		FOOD POISONING DUE TO SALMONELLA		FOOD POISONING DUE TO AEROGENES PARACOLON GROUP		EPIDEMIC-GASTROENTERITIS VIRUS (?)	
			OUTBREAKS	CASES	OUTBREAKS	CASES	OUTBREAKS	CASES	OUTBREAKS	CASES	OUTBREAKS	CASES
1943	28	796	7	178	1	8	1	5			1	47
1944	21	604	4	117			3	16			1	100
1945	9	361	3	173			2	24				
1946	15	656	5	82			2	37			1	300
1947	23	1226	9	239			5	197				
1948	20	513	8	70	1*	86	2	11	2	72		
1949	23	820	9†	144			4	271	1	23		
1950	32	1690	12	325			7	251	1	24	1	615
1951	29	561	7	78			5	181				
1952	54	1409	14	810	3	107	5	97	3	152		
Totals	254	8636	78	2216	5	201	36	1090	7	271	4	1062

Streptococcus faecalis.
†*Micrococcus albus.*

others and exposes the conditions likely to perpetuate recurrence. The history of botulism and mussel poisoning well illustrates the fact that a physician may see, but not understand, illnesses that appear in his community long before an outbreak brings the matter to the attention of the investigator.

Not so long ago gastrointestinal disturbances were often attributable to drinking water contaminated with sewage. Diarrheal disease premonitory to water-borne typhoid epidemics was frequently mistaken for food poisoning. This situation has changed. Not water but food other than milk and its products is the major vehicle for 86 per cent of present-day gastroenteritides. Food is now the core of the problem.

The practitioner, the clinician, is the key person in eradicating food poisoning. He must now give further thought to his concepts of diagnosis and terminology. He must recognize his responsibilities to use the diagnostic laboratory. His superior social consciousness will lighten the additional burdens he is forced to assume by early reporting and by a thorough study of the group illnesses he may suddenly be called on to treat. By so doing he will derive benefit for his patients and for the community in which he serves as the guardian of health.

Prevalence

Before turning to the available data, one must be well aware of what they represent. Some of the difficulties in interpreting them lies in the nature of the outbreaks, and others with the observer. In the first place, there are probably a great many cases, particularly mild individual ones, that do not call for treatment by a physician. If an outbreak does reach the attention of the physician, he frequently cannot obtain samples of the food suspected. Consequently, one food is incriminated because it had been eaten by all persons made ill and not by those not ill, or the organism may be identified by means of symptoms rather than the microscope or test tube. The nature of the outbreak precludes an actual count of the persons affected, so that the report may represent only an estimate. In the reporting, different terms are used differently by different reporters, leaving the interpreter hopelessly bewildered. Laboratories staffed and equipped to identify the responsible agent are not numerous enough, nor are the potential values of available ones realized. Since food poisoning was not reportable in 18 states in 1951, it is impossible to know the absolute prevalence in the United States. The data cannot be treated statistically.

Table 1 (*Concluded*).

Year	Food Poisoning Due to Chemicals		Food Poisoning Due to Plants		Food Poisoning from Unknown Causes		Botulism			Mussel Poisoning
	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Outbreaks	Cases	Proved Cases	Proved Cases
1943					18	558	8	11	1	28
1944					13	371	8	11	4	12
1945					4	164	8	22	5	0
1946	2	156	1	5	4	76	4	6	2	3
1947	1	575	2	11	6	204	3	6	1	0
1948					7	274	3	6	1	3
1949					9	382	1	2	1	0
1950					11	475	5	11	3	0
1951	1	6	1	3	15	293	8	15	4	0
1952					29	243	4	8	2	0
Totals	4	737	4	19	116	3040	52	98	24	46

One must rely on tables compiled by governmental agencies and interested investigators. These furnish information on the known number of persons involved in the annually recurring outbreaks reported in the United States. The United States Public Health Service recently presented tables on reported food-poisoning outbreaks from 1938 to 1951. There was an apparent, steady increase in the number of outbreaks between 1938 and 1949, but in 1950 and, then more pronouncedly in 1951,[6] fewer disease episodes were seen — at least fewer were brought to the attention of this agency. Surprisingly enough, the number of persons affected was approximately the same. The data for the entire country for the year 1952[7] reflect the same trends as those of the previous year. Food poisoning is a reportable disease in California, and the records of the California State Department of Public Health for the past ten years indicate the trends in this state (Table 1). During the first nine years there was no striking reduction, and in 1952 reported outbreaks and cases more than doubled. The reason for the difference between the trends apparent in California records and the United States records is probably twofold: the local and state reporting in California is highly efficient, and the investigative organization, stimulated by the development of a more active epidemiologic intelligence service, is widely used by California physicians. The California report includes 9 outbreaks in 1951 and

24 in 1952 not included by the National Office of Vital Statistics.

Statements that food poisoning is definitely increasing[8] may or may not be correct; at least they are definitely contradicted by the 1951 summary of California's experience. Claims that gastrointestinal disease is a major cause of absence of employees from work[9] can be appraised only when the difficulties in estimating the incidence not in only one state but throughout the country have been overcome.

Feig[1] analyzed the sketchy histories of 987 outbreaks involving 50,819 persons for the years 1945 to 1947, reported by the Milk and Food Branch, Division of Sanitary Engineering, United States Public Health Service. He excluded 61 outbreaks of enteric fever, 14 of bacillary dysentery and 16 of diarrhea, and focussed his interest on 896 outbreaks (involving 42,161 persons) labeled "food poisoning" or "gastroenteritis." About 300 outbreaks were reported each year from not more than 16 states. It is reasonable to suspect that every year the number of persons in the United States who have gastroenteritis more closely approximates several hundred thousand, rather than only about 15,000.

Foods other than milk or milk products are responsible as vehicles for almost 86 per cent of the outbreaks. Contrary to the belief that such outbreaks are more frequent during the warmer months, the evidence tabulated by Feig emphasizes a relatively high number through the remainder of the year — over a three-year period, 114 outbreaks in July, 54 in December and 66 in January.

When one turns to the study of causes, it is disconcerting to observe that in 478 (51 per cent) of the 926 reports of gastroenteritic disease analyzed by Feig (in his Table 2) the etiologic bacterial agent was not determined. Moreover, information about the source of the specimens examined — ingested food or the patient's stool, vomitus or blood — was not available. The causes have not been determined bacteriologically in approximately 46 per cent of the recorded outbreaks in California from 1943 to 1952. This important deficiency is not reflected or readily recognized in the annual summary reports of the United States Public Health Service. For example, only 12 outbreaks among 254 are listed as "miscellaneous or unknown" for the year 1951.[6] However,

TABLE 2. *Food-Borne Outbreaks of Proved and Unproved Causes.*

TYPE	CASES IN UNITED STATES (1947)			CASES IN CALIFORNIA (1943-1952)		
	TOTAL CASES	CASES OF PROVED CAUSE	CASES WITH CAUSE NOT PROVED	TOTAL CASES	CASES OF PROVED CAUSE	CASES WITH CAUSE NOT PROVED
Botulism	12	3	9	52	24	28
Mussel poisoning	—	—	—	46	46	
Chemical poisoning	6	6	—	4	4	
Plant poison	2	2	—	4	4	
Diarrhea	3	—	3	—		
Dysentery	3	3	—	—	—	—
Food poisoning	211*	111	100	242†	126	116
Staphylococcal		100			78	
Salmonella		5			36	
Streptococcal		4			5	
Esch. coli		2			7	
Gastroenteritis	91	46	45	4		4
Staphylococcal		28				
Salmonella		15				
Streptococcal		2				
Esch. coli		1				
Totals	328	171	157	352	204	148

*Outbreaks of proved cause included 74.8 per cent due to staphylococci and 11.6 per cent due to salmonella; no cause was proved in 48.1 per cent.

†Outbreaks of proved cause included 33.3 per cent due to staphylococci and 17.6 per cent due to salmonella; no cause was proved in 42 per cent.

in the narrative text under the heading, "Type of Agent, Staphylococcal Food Poisoning," it is stated that in 63 outbreaks the presence of staphylococci was demonstrated by laboratory tests. Thus, the etiology of 149 (212 less 63) outbreaks was not established. In 1952 California, with 25 etiologically proved and 29 outbreaks of undetermined origin, listed 13 (52 per cent of those of known cause) with the staphylococcal enterotoxin as the most likely cause. It was sometimes shown "microscopically" or by "culture."

For comparison, the excellent reports issued by the British Ministry of Health for 1949[10] and 1950[11] deserve attention. They present a general, not detailed, account of the nature and extent of the problems there. The terms used are defined as follows: outbreaks are 2 or more related cases in persons in different families; family outbreaks consist of 2 or more related cases in members of the same family; and sporadic cases comprise those not related, as far as could be ascertained, to other cases. Each outbreak, family outbreak and sporadic case is con-

sidered as one unit and is reported as an incident. Most striking is the increase in incidence of 64 per cent in 1950 over 1949 (3979 over 2431); sporadic cases increased by 70 per cent, and outbreaks and family outbreaks by 46 per cent in 1950. The higher incidence may be real or may be accounted for by better reporting. Noteworthy is the fact that the number of incidents with no bacterial or chemical cause increased in 1950 by 633. Likewise, the proportion of incidents of unknown causes increased from 36 to 45 per cent (from 874 to 1807). Even in England and Wales, which have an effective reporting system, delay in notification of the health authority has been the reason for failure to determine the bacterial or chemical cause. Contrary to what is generally expected, the proportion of unknown to known causes was not highest for sporadic cases: the percentage of outbreaks of unknown etiology was 51, and that of sporadic cases 46. The vehicle of infection was mentioned in 155 of the 392 outbreaks and was the same type of food — processed or "made-up" meat — recognized in the proved mass episodes of food poisoning.

Etiology

The recent monographs on food poisoning[8, 12] list the following bacteria as the usual causes of outbreaks: staphylococci, salmonella, streptococci, *Esch. coli* and *paracoli*, shigella, *Aerobacter aerogenes* group, *Cl. perfringens (welchii)* and *botulinum*. Probably the most informative tables of proved or presumed causal agents are those in the repeatedly cited paper by Feig[1] and in the British reports of 1949[10] and 1950.[11] Feig's Table 6 is quite specific and detailed concerning the salmonella and shigella, less informative on the streptococci and decidedly incomplete on the staphylococci.

The reports of the outbreaks of food poisoning and gastroenteritis for 1947, one of the years analyzed by Feig, and the bacteriologic findings are summarized in Table 2. One observation stands out clearly: clinical diagnoses are rarely confirmed in more than 50 per cent of the outbreaks. The record is discouraging in botulism: in only 3 of the 12 outbreaks were clostridia isolated, the type being determined in 2 of these. Although the symptoms often implicated staphylococcal enterotoxin as the cause, more than half the histories on gastroenteritis furnish either little or no bacteriologic proof in support of this assumption. More disconcerting is the complete failure to identify the staphylococci presumably involved. Nothing is said concerning the bacteriophage type.

Long dissertations of noteworthy epidemiologic investigations on outbreaks close with the comment that "gram-positive, hemolytic *Staphylococcus albus* was isolated, but facilities were not available for bacteriophage typing or tests for enterotoxin production." In other reports the laconic brevity of the statement that the staphylococcus isolated corresponded "culturally to a food poisoning type strain" borders on the ridiculous. What these criteria may be is obviously not part of the record. Experienced bacteriologists know that nearly all enterotoxin-producing strains fall into two — possibly three — bacteriophage types. If the strain is of some other type or is untypable, its etiologic significance must be regarded as doubtful. Isolation of the same bacteriophage type, both from the patient's vomitus and from the suspected food, is more convincing than that from either alone. Until better facilities are available in some of the state laboratories and until more effort is made to collect specimens suitable for examination, the clamor for specific diagnosis and reporting is meaningless.

Until the percentage of clinical cases of gastroenteritis and food poisoning etiologically proved soars considerably above the present 50, it is premature to implicate the staphylococci categorically as the causal agent in 78 to 82 per cent of outbreaks, even though the data in Table 2 support this contention. Feig[1] states that in the United States staphylococci produce five times as many outbreaks, involving four times as many patients, as the next most common group, the salmonella. The actual incidence of outbreaks arising from the salmonella group is unknown because the nature of the syndrome is such that the only outbreaks reported are those in which fairly large groups of people are involved. The ubiquity of staphylococci, the great variety of foodstuffs in which the enterotoxin is known to have been elaborated and the prevailing apathy regarding prevention of contamination of foodstuffs, however, make a high incidence of staphylococcal food poisoning inevitable. The mere demonstration of staphylococci in food is not adequate proof that the strain is toxigenic and the cause of gastroenteritis.

In Great Britain the diagnosis of staphylococcal gastroenteritis is made less frequently than it is in the United States. Health authorities and physicians there were long unfamiliar with the condition or were skeptical of its existence, so that until quite recently the reports did not reflect the nature or extent of the problem in England and Wales. Instructions and memoranda were issued in 1949 and 1950 on the diagnosis of this disease, including a request for detailed reporting of all single cases of food poisoning,[10, 11] but only 97 incidents (4 per cent) in 1949 and 82 incidents (2 per cent) in 1950 were due to staphylococci. Over 50 per cent of the isolated strains were phage typed, and nearly 80 per cent belonged to one restricted group of types usually associated with illness. The remainder were strains not often associated with food poisoning, and their significance has not yet been ascertained. The infrequent reporting of staphylococcal gastroenteritis in England and Wales may also be partially

explained by the low incidence, but wide distribution, of enterotoxigenic strains.[13] Surveys to determine whether the incidence of toxigenic strains is high in the United States have not been reported and as far as is known have not been attempted. The present interest in staphylococcal gastroenteritis in Italy,[14-16] Holland,[17] France,[18, 19] Germany,[20] Egypt [21, 22] and Russia[23] may furnish information on the distribution of enterotoxigenic staphylococci long before the country in which the etiology of this type of food poisoning was discovered and intensely studied is again aroused to action. Reports from Italy recently pointed out that the role of salmonella there has been reduced in favor of staphylococci.[24]

It has been necessary to devote considerable space to the inadequacy of present-day reporting of outbreaks of food-borne gastrointestinal disease. Unfortunately, all the means to etiologic diagnosis are not available, nor are the available ones used to the fullest extent. Consequently, neither the relative nor, certainly, the actual distribution of the causes of the different forms of food poisoning is adequately presented in the statistics. Since the ultimate prevention is contingent on accurate information regarding the causes and since this information must always originate with the general practitioner, part of the review that follows was prepared with his interest in mind. The term "food poisoning" is used simply for convenience during this transitional period until the illnesses conveyed by food or inherent in it are properly classified. Staphylococcal enterotoxic gastroenteritis, its clinical manifestations and the bacteriology and epidemiology of the illness, which is frequently explosive, involving groups of victims and sometimes only deductively food borne, are discussed. To those familiar with bacterial toxins it is evident that this enterotoxin acts not directly on the gastrointestinal tract but on some specific area in the central nervous system. The nature of the stimulus and the exact location of the susceptible center are not known, but Bayliss[24] has presented important evidence of the pathway and location of the center through the kitten reaction. A study of the action of the toxin on other species, particularly primates, would indeed be invaluable. Salmonella infections are reviewed below under the heading "salmonella gastroenteritis." Less consideration is given to food-borne bacillary dysentery, but the increasingly convincing evidence incriminating *Str. faecalis, Cl. perfringens, Bacillus cereus,* coliform and other organisms will be detailed. Trichinosis is not discussed. Food intoxications with involvement of the central nervous system — botulism, shellfish and fish poisonings — are reviewed.

Staphylococcal Enterotoxic Gastroenteritis

Clinical Manifestations

The symptoms are characteristic and monotonously uniform in most cases. It is common belief that the clinical picture is often so distinctive as to leave little doubt of the diagnosis, even in the absence of bacteriologic proof. This belief is probably largely responsible for the lack of interest in proper diagnosis, at least in the United States. Since the toxin is preformed in food, symptoms appear soon after ingestion. The usual incubation period is 1 to 4 hours, the combined median for 2 outbreaks being 3.35 hours.[25] Most of the outbreaks of known cause with incubation periods of 11 hours or less were of staphylococcal origin. The attack begins with diarrhea and vomiting; the vomiting may be the more conspicuous. Weakness may be prominent, and other symptoms in descending order of frequency include nausea, headache, abdominal pain, leg pains or numbness in the extremities and thirst. Reports on temperature are contradictory; it may be normal, but in severe cases it is often higher. Human volunteers, after ingestion of relatively large doses of toxin, have passed into a state of collapse in which they rest motionless, with cold and clammy skin, shallow respiration and rapid pulse, and a blood pressure of 60 systolic, 20 diastolic. In the more usual episodes the patient improves after 3 to 5 hours or "loses all sense of values and cares not whether he lives or dies." The illness lasts from 0.53 to 2.9 days (median, 1.25 days).[25] The duration may be correlated with the incubation: the illness is long when the incubation is short. Recovery is usually prompt, in from 1 to 5 days, but may be prolonged to a week or two. The account of the subjective aspects by Dolman[13] deserves careful reading by those who have to deal with this disease, particularly since the symptoms described in the published reports vary tremendously. Good descriptions are also offered in the papers by Meyers[26] and in the critical analyses of the available clinical histories by Feig[28] and Kirsner.[27]

The mortality is certainly very low, but 8 apparently authentic fatal cases are on record. Seven of these have been described in the literature,[28-30] and the report of the eighth, in California, has not yet been published. Premature birth and death of an infant after an attack in the mother that was due to eating of fish sausage containing the staphylococcal enterotoxin has been reported.[31] No gross or microscopical pathologic changes were noted. Second and third attacks may occur, but there is evidence that some tolerance to the toxin is established.

There is no specific drug or serum therapy. Treatment is symptomatic. Dehydration is treated by administration of a 5 per cent solution of dextrose or physiologic saline solution intravenously. When the patient can take food without being nauseated, pectin in doses of 3 gm. four times a day, or succinyl sulfathiazole (0.25 kg.), in six doses four hours apart, has been recommended.[32]

The Toxigenic Staphylococci

The role of some types of staphylococci in food poisoning is established beyond question. In fact, a tendency has developed to hold them responsible for almost all explosive outbreaks of gastroenteritis. Until it was shown by the kitten test that some strains of staphylococci grown freely in certain foods give rise to a specific enterotoxin, the early reports on the significance of these micro-organisms were greeted with incredulity.[33] The feline vomiting reaction, ably studied by numerous workers, is not a very accurate test.[34] Nor will the monkey replace the human volunteer, who is so variably susceptible to the enterotoxin. For surveys, animal tests for identifying staphylococcal food-poisoning strains are not only (because of the capricious sensitivity and reaction) unreliable but also expensive when primates are used. Those familiar with experimental staphylococcal gastroenteritis in human beings have encountered either alarmingly severe or only mild indefinite reactions without diarrhea or vomiting. The bacteriologist needs a bench test.

All recent analyses of enterotoxin-producing staphylococci consider the coagulase-positive strains important.[35] Differentiation of serotypes among these cocci has led to the typing of about 98 per cent of the isolated strains. Early beginnings have shown that phage typing, not yet a routine laboratory procedure, may yield more significant findings than serologic tests. About 80 per cent of the strains can be identified; with 22 phages it is possible to classify between 20 and 30 phage types and subtypes of coagulase-positive staphylococci. It is significant that strains from 81 per cent of 47 outbreaks studied in England and Wales belong to only 2 phage types — 6/47 and 42D.[36] Similar observations have been made in Canada: in 10 outbreaks 6 were of Type 6, 2 of Type 42D and 1 each of Type 47 and 31.[37] Phage typing should now be appraised on a much larger scale. One important aspect should be remembered in interpretation of results: 33 per cent of routine stool specimens sent to the laboratory without any suggestion of gastroenteritis contain coagulase-positive staphylococci, probably ingested without ill effects through contact with a nasal carrier or in the daily food. Such findings warn against interpreting as staphylococcal food poisoning any disease in which the same type of staphylococci is found in a food, in the stool of the person who has partaken of it and in the nose or on the hands of someone who has handled it. It is essential that a typical clinical and epidemiologic picture be supported by a count of the viable staphylococci in the suspected food. As strong evidence that staphylococci are responsible it has been suggested that the number of viable, coagulase-positive staphylococci should be about 500,000 per gram of food.[36] The mere contamination of the food with an enterotoxin-producing strain is not sufficient to render the food poisonous.

In culture the medium must promote free growth of the organisms, and the food must be held for a sufficient time at a temperature compatible with growth. The epidemiologist fortunate enough to obtain a sample of the suspected food and the bacteriologist who examines it must consider all these aspects before they venture a diagnosis. Several reports listed in the summaries do not meet critical approval; they cannot be accepted as proved outbreaks of staphylococcal gastroenteritis, their rightful place being in the group of undetermined cause.

Not much is known about the toxin. It has never been prepared in pure form, largely because no satisfactory animal on which to titrate it has been found. There is evidence that in food it has the unusual property of being inactivated more easily by low temperature than by high. It may apparently be destroyed by heating to 65° C. for thirty minutes, but not by boiling for ten minutes. Only long cooking can be relied on to destroy the toxin, and at present, under the encouragement of nutritionists, the trend is away from this type of food preparation.

Vehicles

The most common of the many foods that may purvey staphylococci are meat and bakery products, poultry, potatoes and milk or milk products.[38] Ham, layer cakes, cream and custard pastries are important offenders.[38, 39] Although milk and milk products were recognized long ago, the cow harboring the organisms was often not identified. Recently, Hauge[40] accomplished this epidemiologic feat. Pasteurization does not prevent outbreaks if the products are subsequently carelessly handled.[41] Canned foods of low acid content favoring the growth of staphylococci — for example, meat and fish — have been incriminated in the reports from England and Wales. Of the 76 outbreaks there the vehicle was processed or reheated meat or fish in 59, canned meat or fish in 11, and sweet dishes in 2.[36, 42] Single outbreaks were attributed to dried egg, milk, canned vegetables and fruits. Glazed articles such as pressed beef and brawn are particularly dangerous. Gelatin affords a superb medium for the growth of the staphylococcus, and the melted glaze is usually left to cool at atmospheric temperature. Canned fish plays a role in Russia,[23] and meat soups in Italy.[16] In hot weather the conditions for toxin production are often favorable. A combination of circumstances must be present before this enterotoxin can be formed in food. Such combinations are surely rare in comparison to the number of times food is contaminated with toxigenic strains.

Reservoirs

Early observers equipped with inadequate laboratory tools considered the most likely source to

be the cow.[23, 43] The isolation of enterotoxigenic strains from the udders of cows encouraged this belief.[44] In recent years most investigators of staphylococcal gastroenteritis have come to the conclusion that the most important source of the toxigenic staphylococci is man. The commonest reservoir is the human nose, and a close second is the skin. Minor abrasions may teem with the cocci. Strains involved in outbreaks have been traced to the hands of food handlers. Hobbs and Thomas[45] studied an outbreak stemming from infected lambs' tongues. The staphylococci were of serologic Type 3 (c) and bacteriophage Type 42D, a common food-poisoning type. Investigation of the staff of the canteen where the tongues were handled, instituted on the sixth day after the onset of the outbreak, showed that 11 of 20 workers were contaminated with coagulase-positive staphylococci, but the epidemic Type 3 (c) was found on the hands of one man responsible for slicing the tongues. Two weeks later the skinning and slicing staff were reswabbed, and Type 3 (c) was found on the hands of 4 and in the nose of another. Samples taken seven weeks after the outbreak from various sites in the kitchen yielded Type 3 (c) from two wooden tables and floor dust, suggesting reinfection of the environment by the hand carriers.

Typing

The typing of staphylococci, already discussed in some detail, is just as important as the typing of salmonella. At least one laboratory equipped to type the strains associated with food poisoning should be established in the United States. A technic originally developed in this country by Fisk[46-48] should be given the place it deserves.

Seasonal Incidence

The combination of circumstances to be fulfilled for food to become a vehicle of staphylococcal enterotoxin includes temperature compatible with growth. This has led to the assumption that this disease occurs mainly in the warmer months. Statistics reveal that the incidence remains high even during the colder season.

Prevention and Control

Prevention is fraught with considerable difficulties because the offending organisms are abundant and widespread. Infected food is not altered in appearance, taste or smell, so that the consumer can detect no warning signs. Prevention must depend on general sanitation, general cleanliness and protection of food during preparation and storage. Preventive measures to be taken are outlined in an excellent article by Jensen,[39] and the problems are ably discussed by the discoverer of staphylococcal food poisoning.[12] Nothing can be added to these presentations.

(To be continued)

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MEDICAL INTELLIGENCE

INCARCERATED DIAPHRAGMATIC HERNIA OF THE COLON OCCURRING DURING PREGNANCY

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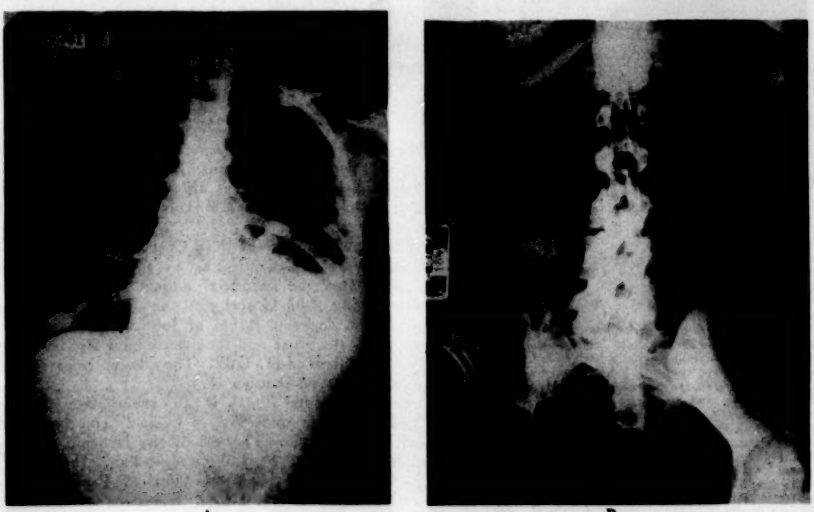
INTESTINAL obstruction during pregnancy is a rare occurrence. Bemis,[1] in 1932, reported 2 cases in 15,000 obstetric patients at the Women's Hospital in New York. Four years later Casagrande[2] reported 2 cases among 11,247 pregnancies at the Brooklyn Hospital. In 1941 Barone et al.[3] reported 5 cases among 45,000 deliveries at the Magee Hospital in Pittsburgh.

Intestinal obstruction due to an incarcerated diaphragmatic hernia is even rarer during pregnancy. Bourgeois,[4] in 1949, reported a case of incarcerated diaphragmatic hernia in which, after a vaginal cesarean section at the thirty-ninth week, a spontaneous cure occurred. He reviewed the literature and found reports of only 8 previous cases, in 5 of which the mothers died. The 3 cases in which the mothers survived were reported by Salgado, who did a section early in labor, by DeLee and Gibson, who described a case with strangulation occurring immediately post partum and responding to conservative treatment, and by Thompson and LeBlanc, who, by an abdominal approach, successfully repaired the strangulation after delivery.



A B

FIGURE 1. *Plain Film* (B) *and Film of the Chest* (A), *Showing Elevation of the Left Leaf of the Diaphragm and Dilatation of the Large Bowel.*

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In the following case an incarcerated diaphragmatic hernia occurred in the first trimester of pregnancy.

H. C., an 18-year-old primipara, entered Cook County Hospital on July 3, 1951, with a 12-hour history of left-lower-quadrant pain and intermittent vomiting. Her last normal menstrual period had occurred "late in March."

Physical examination revealed a young woman who did not appear acutely ill. There was mild tenderness in the right and left lower quadrants. Vaginal examination disclosed a soft cervix, and a uterus consistent with a pregnancy of 3½ to 4 months.

FIGURE 2. *Barium-Enema Examination, Showing Herniation through the Left Leaf of the Diaphragm.*

The temperature was 99.5°F., and the pulse 90. The blood pressure was 150/88.

The diagnosis was intrauterine pregnancy with gastrointestinal upset and possible appendicitis. The patient was sedated and kept under observation. By July 5, she was feeling much better and was no longer vomiting. She was discharged home. Two days later she returned because of a recurrence of the crampy abdominal pain and vomiting. The temperature was 99.6°F., and the pulse 96; the blood pressure was 140/90. There was tenderness in the right and left upper quadrants. The urine showed a trace of acetone. The hemoglobin was 90 per cent (Sahli) and the white-cell count 16,000. Sedation and intravenous infusions of fluids were given, and the next day she was feeling better. She had stopped vomiting, and the abdomen was less tender. On July 9 she stated that she had had severe cramping pain during the previous night. A plain film and a chest film (Fig. 1*A* and *B*) showed the left leaf of the diaphragm to be elevated with dilatation of the large bowel directed toward the left leaf of the diaphragm. An emergency barium-enema examination demonstrated herniation of the large bowel in the region of the splenic flexure through the left leaf of the diaphragm (Fig. 2). The patient was immediately prepared for operation.

Through a thoracic approach, an incarcerated diaphragmatic hernia, comprising a splenic flexure and the left transverse colon, with mesentery and omentum, was noted. The opening in the diaphragm was 1 cm. in diameter in the medial posterior portion of the diaphragm. This opening was enlarged to permit replacement of the hernial contents into the abdominal cavity, and the defect was closed. After operation the patient was given penicillin and streptomycin. The posterior water seal was removed on the 2d day, and the anterior on the 3d day. The temperature, which was 102.5°F. on the 1st postoperative day and 102°F. on the 2d, returned to normal on the 3d. The patient left the hospital on the 10th day. She subsequently carried the pregnancy to term, a normal child being delivered.

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DOCTORS AFIELD

St. Luke, "Most Dear Physician"

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ST. LUKE, one of the four Evangelists and author of the Acts of the Apostles, was a physician. Eusebius,[1] who wrote his *History of the Church* in the fourth century, held St. Luke to have been a native of Antioch, a physician and companion of St. Paul, and separates him from those of the circumcision.

The "beloved physician" or "the most dear physician" is one of several of the Saints honored as a patron of physicians. His versatility is reflected in the fact that he is also the patron of painters (and artists), of glassworkers and (with St. Mark) of notaries.

The writer of the third Gospel is generally represented in ecclesiastical art by an ox or a calf. This connotes the sacrificial animal and signifies the opening of his Gospel with the account of the High Priest Zachary, father of John the Baptist. The book, the brush and the palette have also been used as symbols of St. Luke. The Church celebrates his feast day on October 18.

The name Lucas is an affectionate form of Lucanus, or some say, of Lucius. The name is of Roman origin. The use of the Hellenic Lukas is not accurate. St. Luke was probably the son of a Greek freedman of some wealthy Roman family. He was a Roman citizen. Suetonius mentions that Julius Caesar conferred Roman citizenship on all physicians in Rome. This privilege may have been St. Luke's by inheritance.

The profession of medicine in the first century was quite largely a monopoly of the Greeks. The facile prose of St. Luke's Greek writings and the

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personality that emerges make it probable that he was of Hellenic origin. His tender and extensive discussions of womanhood and infancy have some significance since women and children were regarded as inferior creatures by both Jews and Gentiles of his day.

St. Luke was converted by St. Paul. He became a devoted disciple of the Apostle to the Gentiles and accompanied him on many of his travels and in his ministry. There is some evidence that he attended St. Paul as both friend and physician.

Of the four Gospels, that of St. Luke explains Jewish customs and traditions in greatest detail. He would certainly have had many opportunities for acquiring both Aramaic and Hebrew in his native Antioch.

The writings of St. Luke are characterized by a most meticulous accuracy of detail. His liberal education is clearly apparent in the richness of his vocabulary and in the smooth grace and naturalness of his style. He was a singularly humane and tender being, and his writings breathe the spirit of the Master of Whom he wrote so beautifully.

The Gospel of St. Luke is filled with the spirit of penitence, faith, pity and forgiveness. There is helpfulness, gentleness and kindness in his writings. It is his Gospel that specially seeks out the downtrodden and the despised, the lowly and the outcast. He tells with a compassionate tenderness the stories of the leper, the Samaritan and the publican. Renan called his Gospel "the most beautiful book" ever written.

Various writers have referred to the Gospel of St. Luke and the Acts as a *religio medici*. He expresses in particular degree a profound joy over the triumph of the Savior's "healing art" in overcoming the physical and spiritual ills of men. There are no reliable data available concerning the details of his medical education. It may be conjectured that he studied at the renowned school at Tarsus, which closely rivaled those of Alexandria and Athens.

Much has been written about the "medical" language of St. Luke. Certainly, there is a concise descriptiveness in many of his writings that is entirely consistent with the scientific mind, the trained observer, and the precise recorder. "And there sat a certain man at Lystra, impotent in his feet, a cripple from his mother's womb, who had never walked." (*Acts*: XIV, 7.)

Hobart[1] is the standard authority cited to demonstrate St. Luke's medical background. He points out numerous instances of the use of words and phrases identical with those found in the medical writings of Hippocrates, Aretaeus, Galen and Dioscorides. Harnack says, "It is as good as certain from the subject matter, and more especially from the style of this great work that the author was a physician by profession."

There is nothing in the New Testament lending credence to the tradition that St. Luke was an artist. The Menology of Basil in 980 A.D. and Nicephorus Callistus at a later date refer to him as a painter. Theodorus, who lived about 518 A.D., is cited by Nicephorus as authority for the statement that St. Luke left several paintings of Christ and also of the Virgin Mary. Theodorus is quoted as saying that St. Luke sent a portrait of the Virgin to the Empress Pulcheria, who placed it in the Church at Constantinople. There is a portrait of the Virgin at S. Maria Maggiore in Rome ascribed to St. Luke that has been traced to 847 A.D. An

inscription states, "This is one of the seven paintings of St. Luke." The citizens of Lyons hold the tradition that St. Pothin (d. 177 A.D.) brought with him from the East "an image" of the Virgin Mary attributed to St. Luke.

That St. Luke painted with a brush may not be scientifically established fact. That he painted majestic word pictures is conclusive. His vivid descriptions of the Annunciation, Visitation, Nativity, Shepherds, Presentation, Shepherd and lost sheep and other incidents have long been the inspiration of the great masters.

It is disputed whether St. Luke died a martyr's death. The ancient *Prefatio vel Argumentum Lucae*, dating from the late second century, states that St. Luke was unmarried, that he wrote his Gospel in Achaea, and that he died at the age of seventy-four in Bithynia (probably Boetia) "filled with the Holy Ghost."

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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CASE 39451

PRESENTATION OF CASE

A fifty-five-year-old retired Army engineer was brought to the Emergency Ward because of loss of speech and left-sided paralysis of one day's duration. His landlady gave most of the details of his present illness.

For two weeks the patient had been tired and slightly drowsy at the end of the day. He occasionally had occipital headache; two days before admission the occipital headache was more pronounced, and he went to bed early. The next morning he awoke and felt all right, but within half an hour numbness of the entire left side of the body developed. He had no headache, dizziness or nausea, nor did he vomit or have convulsions. By the end of that day a progressive paralysis of the left arm and leg had developed, and his speech had become slurred. His family physician took his blood pressure, which was 190 systolic, and prescribed nitroglycerin. After taking these pills he vomited and three hours later (four hours before admission) could not talk; his eyes were said to look "in different directions," and his mouth hung open slackly.

One and a half years before the present episode, a sudden left-sided paralysis involving the face, arm and leg developed. He recovered from this without residuum in about two months and resumed work.

On examination the patient was semistuporous and although easily aroused tended to fall asleep. There was ptosis of the right eyelid. He was breathing slowly and at times he seemed to have Cheyne–Stokes respirations. The neck was not stiff. He responded to questions by blinking his eyes. He was barrel-chested, and the lungs were emphysematous; the heart was enlarged, the border extending 4.5 cm. to the left of the midclavicular line. There was a soft blowing systolic murmur at the base radiating to the neck. The prostate was enlarged to twice the normal size but was smooth and firm. Neurologic examination revealed a complete left hemiplegia involving the face, arm and leg. The right fundus was not visualized, but the left was considered normal. The right pupil measured 2.5 mm., and the left 4.5 mm. in diameter. Both pupils reacted to light and near reflex. No field defect was noted. The left eye remained in the midline for all attempted movements to either side. The right eye turned to the right on lateral gaze but not medially. Both eyes could move upward, but when they did vertical nystagmus was elicited. There was slight decrease in hearing on the right. The right side of the palate was flaccid, and the gag reflex was poor. The tongue deviated slightly to the left. The deep tendon reflexes were increased on the left, but all reflexes were brisk. There was a left extensor plantar reflex and left ankle clonus. The plantar reflex on the right was flexor.

The temperature was 101°F., and the pulse 90. The blood pressure was 114 systolic, 76 diastolic.

A lumbar puncture on admission revealed an initial spinal-fluid pressure equivalent to 140 mm. of water; the fluid contained a total protein of 62 mg. per 100 cc. but no white cells. There were some red cells, which were believed due to a traumatic tap. Two later lumbar punctures revealed spinal-fluid pressures equivalent to 140 and 110 mm. of water, with a maximum of 416 red cells and 4 lymphocytes per cubic millimeter each time in the fluid. The white-cell count was 10,000, with 81 per cent neutrophils and 12 per cent lymphocytes. The hemoglobin was 16.0 gm. per 100 cc. The urinary sediment contained a rare granular cast and 1 or 2 white cells per high-power field.

Later in the day examination disclosed a Horner syndrome on the right — a smaller pupil, decreased sweating of the side of the face, ptosis of the lid and slight enophthalmos. The light reflexes and convergence were now normal. The left eye still did not abduct or adduct. A slight unsteadiness in performing co-ordinated movements with the right hand was noted. The corneal reflex was slightly weaker on the left. Although he did not speak, the patient could cough. On the second hospital day divergent strabismus was noted. Paralysis of upward gaze had developed. He was unable to adduct the left eye, but could adduct the right eye slightly. There was a bilateral facial weakness and bilateral palate and tongue weakness, all greater on the left. On the third hospital day upward gaze had returned, with development of coarse vertical nystagmus on upward gaze. On attempted right lateral gaze, the right eye abducted, with development of coarse unilateral horizontal nystagmus, but the left eye did not adduct at all. On attempted gaze to the left both eyes moved well to the left, but gaze could not be sustained. At other times he could not be induced

to look to the left. On the fourth hospital day tachycardia with extrasystoles developed. The temperature rose to 104°F. Blood and urine cultures were negative. He was sweating moderately, with sparing over the right face. The eye findings remained as on the day before. On the fifth hospital day he was comatose, with labored respirations of 24 per minute. The eyes became fixed in the midline, with the right pupil 2.0 mm. and the left pupil 2.5 mm. in diameter; the temperature rose to 108°F., and he died.

Differential Diagnosis

Dr. Richard B. Pippitt*: This seems to be largely a problem of localization of a lesion in the brain.

In summary this middle-aged man had the sudden onset of a left hemiplegia accompanied by cranial-nerve signs, ran a rapid downhill course and died about six days after the onset of symptoms. The association of long-tract and cranial-nerve signs almost certainly puts this lesion in the brain stem. I think there is enough evidence in the record to localize it further and suggest that the bulk of the disease was probably in the pons.

The first point in localization is the bizarre eye movements. The left eye was fixed in the midline and could not abduct or adduct; the right eye abducted but did not adduct. In other words, the significant picture is that of impaired or absent function of the medial rectus muscles on gaze movements. The eyes reacted well to convergence so the fundamental difficulty cannot have been in the innervation of the medial rectus muscles themselves, but rather at a higher level in the co-ordinating centers. The one place a lesion can do this is in the medial longitudinal fasciculus, the tract that co-ordinates the eye movements. The fibers of this tract arise mainly from the vestibular nuclei, run upward underneath the floor of the fourth ventricle and aqueduct, and form synapses with the various oculomotor nuclei. They run downward to synapse with the anterior-horn cells supplying the neck muscles. A lesion in the medial longitudinal fasciculus producing a disturbance in the function of the medial rectus muscles on gaze movements but none on convergence is spoken of as an internuclear ophthalmoplegia.

The problem that bothers me is that, in addition to the lack of adduction of both eyes in gaze, the left eye was fixed in the midline and would not abduct. To explain that I have to postulate a weakness of the left sixth nerve due to injury around the sixth nucleus or possibly a paralysis of left lateral gaze due to a lesion in the corresponding center, which is supposed to be somewhere around the sixth nucleus or above it. The latter lesion could produce paralysis of left lateral gaze, which would interfere with adduction of the medial rectus muscle of the right eye on lateral gaze to the left and also impair the abduction of the left eye. The paralysis of lateral gaze alone, however, will not explain why on right lateral gaze, the left medial rectus muscle failed to adduct. If I am going to say that the patient had paralysis of left lateral gaze, I have to bring in an additional lesion of the medial longitudinal fasciculus on the left to explain failure of the left medial rectus muscle to adduct. I do not believe that it is important to follow all these various deviations and fluctuations in the eye movements, because the changes merely reflected fluctuations in the underlying disease.

At one time he was unable and at another point he was able to look up, but he always had vertical nystagmus — that is, he had impairment of vertical gaze. Normally, we think of vertical-gaze centers as being in the superior quadrigeminal body, but I do not like to put the lesion there because it is a little too far rostral to suit me. I believe I can explain the trouble merely on a pontine lesion that was disturbing circulation to the midbrain and producing these transient difficulties on upward gaze.

The patient also had a Horner syndrome on the right. I was disturbed at the first mention of ptosis because this suggested third-nerve paralysis. It was not until the afternoon of admission that his physicians noted the Horner syndrome. The original ptosis was probably the mild ptosis that we see with Horner's syndrome. He could blink his lids, which would not have been possible with paralysis of the peripheral third nerve. In addition there was evidence that the pupils were small, not dilated, so that the Horner syndrome on the right side was probably due to interruption of the descending sympathetic fibers in the tegmentum.

There was also a paralysis of the palate on the right and weakness of the left side of the tongue. I doubt whether those were primarily nuclear lesions but think that they were due to a disturbance in the corticobulbar tracts, — a pseudobulbar palsy, — which I believe also accounts for the dysarthria or anarthria that was one of the original complaints.

Then I come to the hemiplegia, which started apparently with numbness of the whole left side of the body, followed by steadily progressing left hemiplegia. I should imagine that the numbness was due to disturbance in the medial lemniscus above the decussation and that the left hemiplegia was due to a disturbance in the corticospinal tract, both on the right side in the pons. The increased reflexes and the Babinski sign on the left go with the pyramidal-tract signs.

One point here may or may not be significant: the patient was deaf in the right ear. It is extremely unusual to have deafness from a brain-stem lesion because of the extensive decussation of the fibers. I suppose that slight impairment in one ear from interruption of the lateral lemniscus is possible.

*Assistant ophthalmologist, Massachusetts Eye and Ear Infirmary.

Up to about the third hospital day, all the evidence pointed to a pontine lesion, primarily on the right; then he became worse, and the bilateral signs developed — involving palate, tongue and face. I assume that this was of the upper-motor-neuron type. Rather than put the lesion in specific nuclei, I should prefer to think that this was again interference with bilateral corticobulbar innervation — a pseudobulbar paralysis. The corneal reflex was slightly weaker on the left, probably because of interruption of the fifth nerve's sensory fibers as they crossed, perhaps on the right. I should say that the bulk of the disease was in the pons, perhaps more marked on the right, but it was certainly bilateral at death.

The differential diagnoses to consider are tumor, acute disseminated multiple sclerosis, infection and a vascular lesion. There is very little in this history to suggest either an intramedullary or an extramedullary tumor. The onset was rapid, and the intracranial pressure was not increased. There was no papilledema, and there was no significant elevation in the spinal-fluid protein. Certainly, that is not the picture of a tumor of the posterior fossa. I suppose a queer vascular tumor within the pons that bled or thrombosed is a possibility; I doubt the likelihood of such a tumor.

Acute disseminated sclerosis is quite well ruled out. The patient was fifty-five; although he had some hemiplegia a year before admission, it does not seem likely that multiple sclerosis would have begun at that age. The course was far too fulminating, and nothing in the spinal fluid supports a diagnosis of a demyelinating disease.

There is nothing to suggest an infection — no temperature elevation, no significant white cells in the spinal fluid and so forth.

That leaves me with a vascular lesion, of which the important ones to consider are hemorrhage and thrombosis. The course was not quite fulminating enough to be that of hemorrhage, and there were not enough red cells in the spinal fluid — there were 400 finally, but at the beginning there were none or a very few. Moreover, pontine hemorrhages usually cause death in a matter of hours to a day or two, rather than six days. However, I should not want to rule that out absolutely. The absence of gross blood in the spinal fluid turns me against hemorrhage as a diagnosis.

Embolus I cannot eliminate, but there was no source for it. The heart was enlarged; apparently, its rate was regular and there was only a systolic murmur. I gather that the clinicians were looking for a subacute bacterial endocarditis because blood cultures were done, all of which were negative. I doubt if the patient had subacute bacterial endocarditis. It is unusual for an obstruction to occur in the middle or posterior portion of the large basilar artery from an embolus. The embolus is much more likely to lodge anteriorly where the artery bifurcates.

Thrombosis of the basilar artery, I think, fits the clinical picture best. The patient had vascular disease and a history of a cerebrovascular accident one and a half years before admission, with recovery over a period of months. That, I judge, was a slight thrombosis. I cannot localize it. The prodromes of drowsiness, fatigue and occipital headaches are common with a thrombosis in the posterior fossa. The rapid onset, the drowsiness, the inability to speak and the various long-tract signs associated with cranial-nerve paralysis is extremely common. I shall make a diagnosis, therefore, of thrombosis of the basilar artery that was at first incomplete, more marked on the right, which interrupted the smaller lateral branches of the artery and that toward the end became more complete and more obviously bilateral.

DR. DAVID G. COGAN: The finding that intrigued us in the neuropathology conference was as follows: when the neurologic signs were most reliable there were symptoms pointing to a right-sided lesion in the brain stem — that is, the left hemiplegia and the Horner syndrome on the right; yet the unilateral internuclear ophthalmoplegia pointed to involvement of the left medial longitudinal fasciculus.

DR. PIPPITT: I should think the lesion did involve the left side.

DR. COGAN: In other words the signs indicated involvement of the right pons and the left medial longitudinal fasciculus.

DR. PIPPITT: That would bring the left side in.

DR. COGAN: You would postulate two lesions.

DR. PIPPITT: I think there was paralysis of left lateral gaze and a lesion in the left medial longitudinal fasciculus. I am sure that there was bilateral disease at the onset.

DR. CHARLES S. KUBIK: The right-sided cranial-nerve signs and crossed paralysis of the arm and leg indicated a lesion in the right side of the brain stem. But the internuclear ophthalmoplegia was on the left side, and in view of the post-mortem findings in a case reported a number of years ago,* the lesion responsible for the ocular findings should be on the left side. As Dr. Pippitt has suggested, a thrombus in the basilar artery might block off vessels of both sides even before causing complete occlusion.

CLINICAL DIAGNOSES

Thrombosis of basilar artery, with brain-stem involvement.

Hypertensive heart disease.

Aortic stenosis.

DR. RICHARD B. PIPPITT'S DIAGNOSIS

Thrombosis of basilar artery, with bilateral infarction of pons.

*Cogan, D. G., Kubik, C. S., and Smith, W. L. Unilateral internuclear ophthalmoplegia: report of eight clinical cases with one postmortem study. *Arch. Ophth.* 44:783-796, 1950.

Anatomical Diagnoses

Thrombosis of fusiform (atherosclerotic) aneurysm of basilar artery.
Infarction of pons, bilateral.
Hypertensive heart and coronary-artery disease.

Pathological Discussion

Dr. Edgar B. Taft: At autopsy the findings, as postulated, were largely confined to the brain; however, there was a moderate cardiac hypertrophy, consistent with hypertensive heart disease. The coronary arteries were moderately atherosclerotic, and there was a small amount of myocardial fibrosis. Two interesting but apparently clinically unsuspected incidental findings were present; these were

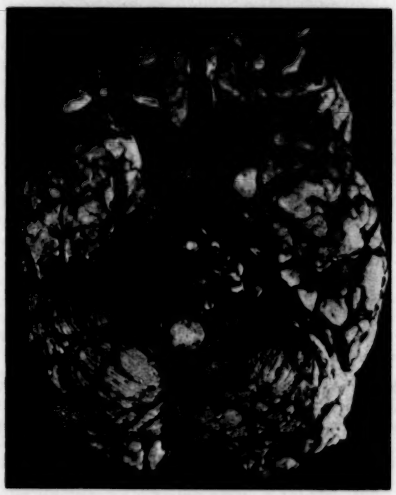

Figure 1. *Undersurface of the Brain, Showing the Basilar Aneurysm.*

active pulmonary tuberculosis and active tuberculosis of the mediastinal lymph nodes. The lesions in the lungs were somewhat calcified but still moderately active; those in the lymph nodes were very active, with caseous necrosis. The gall bladder was packed with stones.

Dr. Edward P. Richardson, Jr.: Dr. Pippitt was quite correct in his prediction that thrombosis of the basilar artery, with infarction of the pons, would be discovered. All the large cerebral arteries were extensively atherosclerotic. The basilar artery was widely dilated, maximally to approximately 1 cm. in diameter, and pursued a tortuous S-like course (Fig. 1). This is the typical picture of arteriosclerotic aneurysm of the basilar artery — the term "aneurysm" in this case implying a fusiform dilatation of the entire length of the artery, presumably as a result of atheromatous degeneration of the walls. The aneurysm was filled with thrombus which for the most part looked recent.

In the base of the upper third of the pons on the right side was a small cavity, characteristic of old infarction. This undoubtedly was the cause of the transitory left hemiplegia one and a half years before the final episode. This cavity was surrounded by extensive recent infarction, which involved almost the entire right side of the base of the pons. There was likewise recent, less extensive necrosis of the base of the pons on the left. These bilateral lesions thus accounted for the bilateral neurologic signs. There was an additional small lesion in the tegmentum of the pons on the left, which occupied the exact site of the medial longitudinal fasciculus at a level above the nucleus of the abducens nerve and

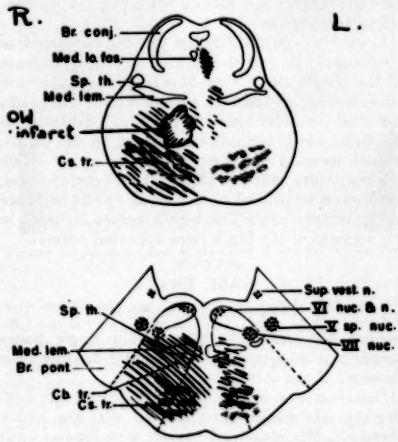

Figure 2. *Diagram of the Location of the Lesions in the Pons. (The Cross-Hatched Areas Represent Recent Infarction.)*

below the nuclei of the oculomotor and trochlear nerves. The brain-stem infarction was confined to the pons and did not extend upward into the midbrain or downward into the medulla oblongata (Fig. 2). There was in addition a small area of recent infarction in the right cerebellar hemisphere—probably giving rise to the slight impairment of co-ordination in the right arm.

Dr. Pippitt's excellent discussion points out clearly the relation of the clinical features of this case with the pathological lesions. The infarction on the right side of the base of the pons involved the medial lemniscus and enough of the adjacent tegmentum (with the descending sympathetic fibers) to account for the left-sided "numbness" and the right-sided Horner syndrome. The lesions on the

left undoubtedly came close enough to the pontine center for lateral gaze (in or near the abducens nucleus) to cause the transitory paralysis of left lateral gaze, although this area was not visibly damaged. The failure to adduct the left eye on attempted right lateral gaze, with preservation of adduction on convergence, — that is, left internuclear ophthalmoplegia, — is explained by the lesion in the left medial longitudinal fasciculus. It is to be noted that the impaired adduction occurs on the same side as the lesion. This likewise occurred in the only previously reported case with adequate pathological confirmation referred to by Dr. Kubik.

The history does not give any clinical manifestations that can be related to the aneurysmal dilatation of the basilar artery. We must assume that it was asymptomatic until thrombosis occurred within it — whereupon the picture was that of basilar-artery thrombosis.

Since brain-stem infarction can be considered as a rule never to give rise to loss of hearing because of the many alternative fiber pathways that are available to the auditory system within the brain, one might wonder whether the slight deafness on the right was the result of pressure on the eighth cranial nerve by the distorted basilar artery. This is a possibility that can be raised for consideration, but cannot be proved or disproved by the evidence in the present case. The eighth nerves included in our sections of the brain stem appeared normal.

CASE 39452

Presentation of Case

First admission. A fifty-year-old single bookkeeper was admitted to the hospital because of a "tumor" of the uterus.

One year previously, during a general physical checkup, the patient first learned that she had a "tumor." Her menstrual periods were regular until one and a half years before admission, when they ceased. There was an isolated menstrual period seven months and then another profuse one two months before admission.

On bimanual examination a large, nodular uterus was palpated. The remainder of the examination was negative.

Laboratory studies were negative.

On the second hospital day an abdominal laparotomy was performed. The uterus was small, but the fundus contained a firm tumor mass. The ovaries were atrophic, and both tubes and ovaries were sealed over and plastered down along the posterior surfaces of the broad ligament with very dense adhesions. A total hysterectomy and bilateral salpingo-oophorectomy were done. Examination of the uterus disclosed a polypoid mass filling the endometrial cavity. Subsequent reports by the pathologist were as follows: "1. Adenocarcinoma, Grade 3, of the endometrium with invasion of the myometrium. The serosa of the uterus appears to be free of tumor, although tumor invading the myometrium extends to within about 0.3 cm. of the serosal surface. 2. Tuberculous salpingitis."

The postoperative course was uneventful, and the patient was discharged on the twelfth hospital day.

Second admission (two weeks later). While in the hospital she had had some discomfort behind the right knee without objective signs of phlebitis.

Figure 1. *Roentgenogram of the Chest Taken Twenty-Seven Months before the Final Admission.*

After discharge she felt well until five nights before admission, when she suddenly felt weak and lightheaded while watching television. She had no other symptoms except mild aching of the right leg, including the anterior part of the knee and lateral aspect of the lower leg. This was accompanied by visible swelling. Two nights before admission generalized malaise and weakness without fever or chills developed. She had interscapular back pain but no chest pain, cough or hemoptysis. She continued feeling poorly without specific complaints.

On physical examination she appeared chronically ill and slightly pale. Aside from proximal tenderness and soreness medial to the femoral artery on the right and tenderness over the lateral aspect of the right leg, the examination was negative. The temperature, pulse and respirations were normal.

A roentgenogram of the chest revealed fibrocalcific scars in both apexes, but was otherwise normal (Fig. 1).

The patient was given Dicumarol for three days and discharged three days later in the absence of more definite findings.

Final admission (twenty-seven-months later). In the interval she was well until a month before ad-

mission, when she noted the rather sudden onset of pain and weakness in both lower extremities, back and lower abdomen, which prevented her from climbing stairs. The acute pain subsided, but pains persisted in the lower abdomen and in both groins and thighs. During the last two weeks before admission obvious swelling of both lower legs had developed. She had continued to work but had been increasingly troubled with swelling and pain in the legs. She did not have frequency, dysuria or hematuria. She had had intermittent pain in the lower abdomen throughout the two years since operation, and this had been much worse during the past month. She had been somewhat constipated during the three months and had experienced shortness of breath on climbing stairs during the three weeks before admission.

On physical examination the patient was not in acute distress. The thyroid gland was enlarged to twice the normal size, and there was a solitary palpable nodule in the lower pole of the left lobe. There were no signs of hyperthyroidism. The heart and lungs were normal. In the abdomen there was spasm and rebound tenderness in both lower quadrants, and the liver edge was felt 1 or 2 finger-breadths below the costal margin. On pelvic examination there was no vaginal bleeding or discharge. There was diffuse tenderness in the vaults and cul-de-sac. Rectal examination was noncontributory. The legs were swollen, tense and shining, with pitting edema. There was diffuse tenderness and induration over the medial aspects of the thighs proximally.

The temperature was 99°F., and the pulse, respirations and blood pressure were normal.

The urine was normal. Examination of the blood disclosed a hemoglobin of 8.7 gm. per 100 cc. and a white-cell count of 6700, with a normal differential count. The sedimentation rate was 56 mm. in sixty minutes. The serum total protein was 6.7 gm., the albumin 3.7 gm., the globulin 3.0 gm., and the nonprotein nitrogen 16 mg. per 100 cc.; the prothrombin time was 14 seconds (normal, 14 seconds). Two vaginal smears were unsatisfactory; one was negative.

A roentgenogram of the chest showed moderate displacement of the trachea to the right in the lower portion of the neck. The superior mediastinum appeared definitely wider than at the time of the previous examination. There was also evidence of subcarinal adenopathy (Fig. 2). A barium-enema examination was negative except that the large bowel, rectum and distal sigmoid colon were somewhat displaced to the right and of narrower caliber than usual. However, there was no obvious infiltration of the rectal wall. A plain film of the abdomen taken two weeks after admission appeared to be normal.

In the hospital while the patient was at bed rest and on Dicumarol therapy there was a gradual loss of edema of the legs, and by the fifteenth hospital day there was no ankle edema or evidence of phlebitis. However, tenderness over the lower abdomen persisted. A second x-ray film of the chest and barium-enema examination done about three weeks after admission were unchanged. At about the same time, while she was still on anticoagulants,

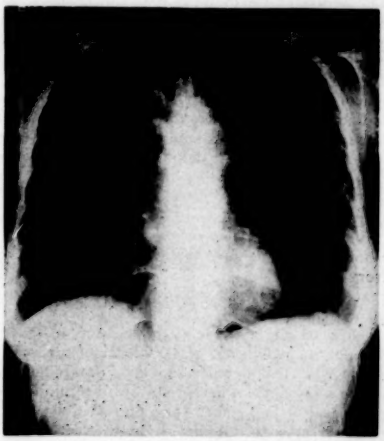

FIGURE 2. *Roentgenogram of the Chest Taken during the Final Admission.*

her entire left leg became uniformly swollen and did not pit except over the instep. It was also hot, red and exquisitely tender. It improved after several days; however, she continued to appear ill and complained bitterly of shifting pain in the legs and abdomen. The chest remained clear. She was discharged slightly improved after about a month in the hospital. The temperature curve had been irregular, with almost daily elevations to 99° or 99.5°F., although a leukocytosis had never developed.

At home her condition remained about the same. The legs again became swollen, and terminally she became irrational. She died about two weeks after discharge from the hospital.

DIFFERENTIAL DIAGNOSIS

DR. GORDON S. DONALDSON*: This is a long and difficult case. The information may be condensed to a report of a fifty-year-old woman who had a proved carcinoma of the uterus for which she had a hysterectomy, who developed in all probability a thrombophlebitis of the right leg, and who later deteriorated rather rapidly. Prominent in the picture at that time was massive swelling of the legs, and lower abdominal spasm. Dangerous as it is at these meetings to make two diagnoses, I am going

*Assistant surgeon, Massachusetts General Hospital.

to do so here. One may be secondary to the other. Trousseau[1] pointed out many years ago that patients with cancer, particularly those in the "cancer age group," often herald their disease by exhibiting thrombophlebitis or pulmonary embolism. I do not think anyone has adequately explained why phlebitis develops in such cases. Trousseau originally associated the phlebitis with cancer of the pancreas. In the last couple of years, there has been a great deal of work with trypsin in both the production and the therapy of thrombophlebitis. Trypsin may be a factor in the development of phlebitis in patients with cancer of the pancreas, but in other types of cancer, such as that of the breast or bowel, it is possible that the cancer exerts its effect through the bone marrow, the liver or the reticuloendothelial system to initiate changes in the blood-clotting mechanism that result in thrombophlebitis.

Since there are one or two bothersome details, before proceeding any further, I should like help from the radiologist. This nodule, for instance, that developed on the left lower lobe of the thyroid gland and later produced displacement of the trachea to the right may have been malignant. I doubt it. Also, there was evidence of tuberculous salpingitis. The patient had a good deal of evidence in the x-ray films of healed apical tuberculosis. Did peritoneal or pulmonary tuberculosis enter into the terminal episode? Again, I doubt very much if pelvic tuberculous peritonitis could produce such massive edema and such symptoms in the lower abdomen. Lymphedema as the result of the operation also seems unlikely. I wonder if we could look at the barium-enema examination and chest films? The widening of the mediastinum was described as developing in the course of two years.

DR. JOSEPH HANELIN: The two chest examinations, about a year apart, the last of which was two years before the final admission, show essentially the same findings (Fig. 1). There was a fairly normal mediastinal shadow at that time and evidence of old scarring, probably tuberculous, in both upper-lung fields. At the time of the final admission, however, a distinct change has occurred (Fig. 2); the mediastinum is now wider than it should be; this appears to be the result of enlarged paratracheal lymph nodes. There is also evidence of enlargement of the subcarinal lymph nodes. The pulmonary apical lesions are unchanged. The trachea is displaced slightly to the right side. Two barium-enema examinations a few weeks apart, at about the time of the last admission, show similar findings. There is no intrinsic lesion of the colon; however, there is some displacement of the rectum and distal sigmoid to the right side (there was tenderness in this area). There may also be some fixation of the sigmoid, but again no intrinsic disease. In a lateral projection, the rectum lies more anteriorly to the sacrum than usually does.

DR. DONALDSON: By quite a good deal?

DR. HANELIN: Yes.

DR. DONALDSON: This patient reminds me very much of one who entered the hospital about three years ago with vaginal bleeding having been given Dicumarol for thrombophlebitis of the left leg. Eventually, dilatation and curettage were done, endometrial cancer was found, and she had a panhysterectomy. About two and a half years later the tumor recurred, and she died of recurrent pelvic cancer. A severe degree of leg edema developed over the terminal three years of life, presumably because of pressure on the pelvic veins and lymphatics by tumor.

I think, however, that there is adequate evidence that the patient under discussion had thrombophlebitis in addition. The physicians who took care of her apparently thought she had thrombophlebitis and treated her for it very well. The pain behind the right knee on the first admission was not in a usual site for thrombophlebitic pain to make its appearance. We are more likely to see such pain in the instep, forefoot or calf, although a good report from Canada[2] a couple of years ago stated that in 73 per cent of cases of thrombophlebitis the process first appeared in the thigh or pelvis. Our figures are not that high, and the discrepancy is probably due to the fact that the Canadian statistics are based on autopsy material. A patient who has been on the operative table or in stirrups for a dilatation and curettage is apt to develop symptoms initially in the popliteal space. This patient did have swelling during the second admission, and although no fever was recorded, I believe that fever is not essential. The leg was tender, particularly over the femoral lymph nodes medial to the femoral artery, a sign that is often overlooked. She was given Dicumarol for only three days and then went home and got along perfectly well. Many might agree that she probably would have been as well without the Dicumarol. Only about 10 per cent of the patients in this hospital with an established, diagnosed thrombophlebitis have emboli, and few of these have fatal emboli. In summary, I think it can be safely said that before the third admission this patient had thrombophlebitis of the right leg.

Twenty-seven months later at the time of the final admission she had marked symptoms. The pain was more severe than I should like to see it for the diagnosis that I am entertaining, and so were the tenderness and spasm in the lower abdomen. She also had pain in the groin and thigh, some swelling of the legs and tenderness of the femoral vessels, elevation of the sedimentation rate and slight fever. Looking at the leg alone, I might believe that most of the trouble came from that source. However, I believe that she also had recurrent cancer.

There are several points in favor of recurrent cancer. Dr. Joe V. Meigs has said many times that one cannot tell at operation, by looking at the pelvis or even by palpating the lateral pelvic regions, whether a patient has metastatic involvement of the pelvic lymph nodes. One has to resect such areas to make sure that no disease exists in the lymph nodes. He has also pointed out that some patients with endometrial cancer have metastases to the lymph nodes in the lateral areas, the result of spread along the uterine, hypogastric and iliac arteries to the common iliac or the obturator lymph nodes. So there is a good chance that at the time of the original operation this patient had disease that was beyond the confines of the total hysterectomy. Finally, the widening of the mediastinum means to me that she had disease through the aortic lymph nodes and on up into the mediastinal area. The displacement of the rectum could have been due to either thrombophlebitis or cancer. It would take a large amount of cancer to displace the rectum that much. On the other hand a pelvic thrombophlebitis with involvement of the hypogastric vein would produce enough edema to give the bowel a stiff appearance at fluoroscopy and displace it as it was displaced here. I believe this could be settled only by the pathologist. Another point, which is at best a small one, is that emboli occur in the presence of an adequately depressed prothrombin time; however, I do not think there is often a progression of swelling. While she was on anticoagulants, she had a flare-up of her leg symptoms. There was much more pain, and a shiny, tense leg developed. The final anemia that appeared may also have been due to recurrent carcinoma. I am not sure I should try to say just what was where, but I believe this is the sort of case that Trousseau[1] himself would have been delighted to see and perhaps would have included in his series.

Dr. Benjamin Castleman: Did you say what was going on in the lung?

Dr. Donaldson: I think there was no disease in the pulmonary parenchyma.

Dr. Hanelin: I can tell you what we thought about it. There was evidence of old pulmonary tuberculosis so we considered that this might be tuberculous adenopathy. There were two other possible sources of enlargement of the lymph nodes: thyroid cancer and metastases from the endometrial carcinoma.

Dr. Donaldson: Another possibility is a thrombosis of the inferior vena cava. This woman did have iliac thrombosis, and may have had extension to the vena cava. The occlusion usually is not complete, but subtotal. I think that is rather farfetched.

Clinical Diagnosis

Phlebitis, pelvic and peripheral.
?Recurrent carcinoma.

Dr. Gordon S. Donaldson's Diagnoses

Recurrent carcinoma.
Pelvic thrombophlebitis.

Anatomical Diagnoses

(*Adenocarcinoma of uterus, Grade 3*), *with metastases to abdominal, pelvic, and thoracic lymph nodes, invasion and occlusion of inferior vena cava and obstruction of right ureter.*

Tuberculosis, healed, lung apexes, bronchial and porta-hepatis lymph nodes (and tuberculous salpingitis).

Multinodular colloid goiter.

Pathological Discussion

Dr. Castleman: Autopsy showed that some enlarged lymph nodes in the mediastinum were due to old tuberculosis, but most of them were due to metastatic carcinoma that looked microscopically very much like the original carcinoma of the endometrium. The patient did have a massive involvement of the retroperitoneal lymph nodes. The entire pelvis was filled with recurrent cancer, which had invaded the veins; both the iliac veins were occluded with both bland and tumor thrombi; the inferior vena cava up to 2 cm. from the renal veins was almost completely filled with tumor thrombus, undoubtedly accounting for the massive edema that she had during the last admission. Dr. Donaldson's statement about involvement of the inferior vena cava was really not so far-fetched. The thyroid gland showed a nontoxic nodular goiter. There was healed tuberculosis in the lungs and lymph nodes but no activity and nothing in the lungs of a neoplastic nature.

Dr. Donaldson: How often do you see venous invasion by endometrial carcinoma?

Dr. Castleman: It is not common. The lymph nodes along the aorta and vena cava were so large that I think the tumor thrombi extended from an involved lymph node into the vena cava.

Dr. Farahe Maloof: Were the subcarinal lymph nodes involved?

Dr. Castleman: Yes; they were all neoplastic and formed a mass about 7 cm. in diameter.

Dr. Maloof: Is that not unusual with metastatic disease from outside the chest?

Dr. Castleman: If metastases involve the abdominal para-aortic lymph nodes, they frequently pass through the diaphragm to involve lymph nodes in the mediastinum. For example, it may occur with cancer of the body of the pancreas, and one or two such patients have come into the hospital with a diagnosis of mediastinal lymphoma.

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MORE ABOUT CARBOMYCIN

IN a previous editorial[1] dealing with carbomycin (Magnamycin), a summary was given of the clinical reports of its use available at the time; the results indicated that this antibiotic had no particularly favorable effects on many infections with organisms that were highly sensitive to its action in vitro. In addition, it was noted that assays of blood and urine from patients under treatment with this agent failed to demonstrate significant concentrations of active antibiotic, and this may have accounted for the poor clinical results.

Carbomycin could not therefore be recommended as a potentially useful drug for the treatment of bacterial infections. It was considered to be specifically contraindicated in the treatment of pneumococcal pneumonia because several other more effective agents are available for this disease and because particularly unfavorable results had been obtained in a number of cases treated in Boston and Syracuse (details of the latter cases were recently reported by Bunn and Cook[2]). Nevertheless, a large proportion of patients in the same and other clinics recovered fairly soon after treatment with this agent. The results of the treatment of acute streptococcal pharyngitis appear to be more favorable, at least according to the report by Bigham, Jones and Manning presented elsewhere in this issue of the *Journal*. Their results must also be weighed against the decidedly superior effects of other antibiotics, particularly penicillin, in these infections and also against the fact that increased resistance of Group A streptococci to these effective antibiotics has not been encountered clinically. The results in the cases of acute gonorrheal urethritis treated with carbomycin were clearly unfavorable.

The favorable effects of carbomycin in amebiasis were also commented on previously, and its possible usefulness in infestations with this and other intestinal parasites was considered worthy of further exploration. In a recent study on the clinical pharmacology of carbomycin, Brainerd and his coworkers[3] obtained high serum concentrations that persisted for twelve hours or more in jaundiced patients, in contrast to the low or negligible levels in patients without jaundice. Concentrations approximating those of the serum were also found in ascitic fluid in most of the cases studied. The authors therefore suggest that carbomycin may offer a promising therapeutic approach to infections of the hepatobiliary system by susceptible pathogens, including *Endamoeba histolytica*.

Another possible area of usefulness for carbomycin is suggested in a report from Harlem Hospital[4] on the use of this agent in certain venereal diseases. In this study, as in others, carbomycin was found to be much inferior to other antibiotics, particularly penicillin, in the treatment of acute gonorrhea, in spite of the fact that the strains of gonococcus isolated were highly sensitive in vitro. Carbomycin also had no beneficial effect in cases of lymphogranuloma venereum although the causative agent of this disease is also said to be susceptible. On the other hand, highly encouraging results were obtained

in 8 acute cases of granuloma inguinale treated with either 1 gm. twice a day by mouth or 500 mg. intravenously once daily. Complete healing occurred in 5 cases after treatment for twelve to twenty-eight days, and evidence of healing was noted in the other 3 cases after three days of therapy. Typical Donovan bodies were demonstrated in exudate from the lesions in every case before carbomycin therapy was started. Streptomycin, chlortetracycline and oxytetracycline have also been found to be effective in this disease. Nevertheless, these results are of considerable interest, not only because they offer another potentially effective agent and may provide some insight into its mode of action but also because the causative organism of this infection is biologically quite distinct from all other pathogenic micro-organisms for which antibiotics have been found useful.

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THE MARCH OF MEDICINE

To the Boston group went the distinction on October 8 of inaugurating the first televised program on the new "March of Medicine" series. The March of Medicine is under the sponsorship of the American Medical Association and Smith, Kline and French Laboratories; the first presentation of the series, a progress report on the campaign against heart disease, was prepared in co-operation with the Massachusetts Medical Society, the Massachusetts Heart Association and the faculties of Harvard Medical School, Boston University School of Medicine and Tufts College Medical School.

The participants were Dr. Herrman L. Blumgart, professor of medicine at Harvard Medical School and physician-in-chief of the Beth Israel Hospital, and his associates, Dr. A. S. Freedberg and Dr. Paul M. Zoll; Dr. Howard B. Sprague, clinical associate in medicine at Harvard Medical School and former president of the American Heart Association; Dr. Paul D. White, consultant at the Massachusetts General Hospital and executive director of the National Advisory Heart Council; Dr. Robert W. Wilkins, associate professor of medicine at Boston University School of Medicine and certain of his associates; Dr. Edward J. McCormick, president of the American Medical Association; and Fred Allen, who played the part of a hypertensive patient.

This practice march, so to speak, was of interest to physicians who viewed and approved it and to various laymen who commended it and believed that it accomplished its purpose of making clearer some of the problems of cardiologists and at the same time presenting the encouraging facts of heart disease. Certain features, such as the actual moving-picture shots of a thrombus forming within a vessel, were obscure to a lay audience. In the same category was the excursion made by the intrepid president of the American Medical Association into the chambers of a mammoth model of a heart, where he described its topography. He might as well have been inside the Carlsbad Caverns except for the superior lighting of the latter. Both the thrombotic phenomenon and the anatomic presentation would have been better illustrated by simple diagrams.

These, however, are minor criticisms that may help another time in an even better employment of the thirty precious minutes allotted to this program. The presentation as a whole was impressively simple, clear and dignified and represents one of the best efforts yet made in the establishment of sound public relations.

The program on November 5 reports on cancer research, and that on December 3 will present the highlights of the meeting of the American Medical Association in St. Louis.

NEW INSURANCE PLAN

The sales campaign being conducted by the C. O. Finley Company of Chicago and Boston as agents for the Lumbermen's Mutual Casualty Company offers fellows of the Massachusetts Medical Society who would otherwise be unable to purchase accident and health insurance an opportunity to do so, provided that at least 50 per cent of the members enroll.

The Society, by vote of the Council, authorized this campaign. It does not thereby exclude other insurance companies from doing the same thing, although no other companies have submitted proposals. The councilors voted to give the members an opportunity to familiarize themselves with the plan.

The insurance committee of the Society recommended the policy offered, but as President Hagler pointed out in his introductory letter, the need for the protection and the desire to participate is an individual decision. All insurance policies are not alike; some have weaknesses not apparent in others, and some have advantages not offered in others. Before canceling any satisfactory policy he now owns, a fellow is only exercising common sense if he carefully studies the provisions of both old and new policies and seeks the guidance of a disinterested insurance counselor as well as that of the agents of the several companies. Mr. Reed Geise, 808 Park Square Building, 31 St. James Avenue, Boston, represents the C. O. Finley Company and will be glad to offer his advice.

The Massachusetts Medical Society is only one of a number of physicians' organizations that have co-operated with accident and health insurance companies to enroll their members in similar plans. Such plans may fail to fulfill their apparent obligation if, owing to the financial risk of carrying elderly and infirm physicians through prolonged illness or because of an unusual number of claims for reimbursement by policy holders, the insurance companies find the plans unprofitable. This could result in increased rates or even in cancellation of agreements entered into in good faith by both parties.

DETECTION OF DIABETES

Diabetes Week, the culmination of the efforts of the American Diabetes Association to stimulate public interest in the detection of diabetes, begins this year on November 16. Locally, the high spot of the week will be the sixth annual Diabetes Fair, whose general purpose is discussed by Dr. Harry Blotner, chairman of the Committee on Diabetes Detection of the New England Diabetes Association, in correspondence published in last week's issue of the *Journal*. In addition to Dr. Blotner, the committee in charge of the Fair includes Drs. Frank N. Allan, Charles W. Finnerty, Alexander Marble and Howard F. Root. The officers of the New England Diabetes Association are Dr. Richard P. Stetson, president; Dr. Reed Harwood, vice-president; Dr. Tillman McDonald, treasurer; and Dr. C. C. Bailey, secretary.

As in previous years, both the public and the medical profession are urged to take part in the two-day program of displays, motion pictures, lecture programs and panel discussions, as well as the interesting and valuable procedure whereby tests for sugar in the urine and blood are performed with the subjects as witnesses. The Diabetes Fair especially deserves the support and encouragement of physicians, some of whom, it is disheartening to note in Dr. Blotner's letter, are not equipped to perform urinary tests for sugar on their patients. The opportunity of watching the technic of sugar detection and at the same time, by education of the public, of helping to uncover the estimated 1,000,000 undiscovered cases of diabetes in the United States should not be neglected.

From the account received from Carlsvrona, in Sweden, it will appear that the immense havoc which the cholera has made has been in a great measure attributed to the bad quality of the water.

Boston M. & S. J. *November 9, 1853*

MASSACHUSETTS MEDICAL SOCIETY

BRICKER RESOLUTION

The Council of the Massachusetts Medical Society has instructed the Committee on National Legislation to support the so-called Bricker Resolution (S. J. Res. 1). During the discussion of this matter in at least one district pre-council meeting it appeared that few if any councilors had read the resolution under discussion.

For the information of fellows of the Massachusetts Medical Society, the resolution, as amended on June 15, 1953, is presented herewith:

JOINT RESOLUTION PROPOSING AN AMENDMENT TO THE CONSTITUTION OF THE UNITED STATES, RELATING TO THE LEGAL EFFECT OF CERTAIN TREATIES AND EXECUTIVE AGREEMENTS

SECTION 1. A provision of a treaty which conflicts with this Constitution shall not be of any force or effect.

SEC. 2. A treaty shall become effective as internal law in the United States only through legislation which would be valid in the absence of treaty.

SEC. 3. Congress shall have power to regulate all executive and other agreements with any foreign power or international organization. All such agreements shall be subject to the limitations imposed on treaties by this article.

SEC. 4. The Congress shall have power to enforce this article by appropriate legislation.

SEC. 5. This article shall be inoperative unless it shall have been ratified as an amendment to the Constitution by the legislatures of three-fourths of the several States within seven years from the date of its submission.

ROBERT W. BUCK, M.D.
Secretary

BOOK REVIEW

Physical Examination of the Surgical Patient. By J. Englebert Dunphy, M.D., and Thomas W. Botsford, M.D. 8°, cloth, 326 pp., with 188 illustrations Philadelphia: W. B. Saunders Company, 1953. $7.50.

This book, as the authors point out in the preface, is intended primarily for the medical student and the general practitioner. It will also be read with interest and profit by anyone concerned not only with surgery but also with physical diagnosis. The features and technic of physical examination are clearly described, with numerous detailed sketches, in terms of normal and disordered physiology, knowledge of the former being essential in the discovery of the latter. The object of physical examination, which is regarded as the fundamental principle of surgical diagnosis, is defined as the detection of the presence and extent of injury or disease by means of the eyes, ears, fingers, nose and brain of the examiner. At the same time, some simple fundamentals of medicine and surgery are emphasized, and the patient is considered in terms of sympathy and understanding, with respect for his individual differences from his fellows.

An important section of the book includes the examination of the injured patient. Also, a check list, contained in an appendix, offers a useful index to the various components of the physical examination. The book cannot fail to be of great value to all students and practicing physicians.

CLAUDE E. WELCH, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Pain Syndromes and Their Treatment: With special reference to shoulder-arm pain. By James M. Tarsy, M.D., chief, Arthritis Clinic, University (New York Postgraduate) Hospital, New York University-Bellevue Medical Center, associate visiting physician, Bellevue and University Hospitals, assistant clinical professor of medicine, Postgraduate Medical School, New York University, New York, New York, and chief, Arthritis Clinic, St. Mary's Hospital, Brooklyn, New York. 8°, cloth, 592 pp., with 266 illustrations. Springfield, Illinois: Charles C Thomas, 1953. $12.00.

Dr. Tarsy has written a comprehensive book on pain. The text is divided into general considerations and methods of examination; pain syndromes in cervical lesions, thoracic lesions, shoulder lesions and peripheral lesions; and treatment. Lists of references are appended to the chapters, and there is an auxiliary bibliography. There is a good index, and the publishing is excellent. The book should be in all medical libraries and in the collections of neurologists and orthopedists.

National Health Insurance and Alternative Plans for Financing Health. By Seymour E. Harris, professor of economics, Harvard University. With a foreword by Alfred B. Lewis. 8°, paper, 40 pp. New York: League for Industrial Democracy, 1953. $0.25.

Professor Harris expresses his preference for national health insurance. He discusses its cost and economics, the supply of physicians and the problem of financing the medical schools, and voluntary insurance *versus* federal insurance.

Poliomyelitis. By W. Ritchie Russell, C.B.E., M.D. (Edin.), M.A. (Oxon), F.R.C.P. (Edin.) and F.R.C.P. (Lond.), consultant neurologist to the United Oxford Hospitals, consultant neurologist to the Army, consultant neurologist to the Ministry of Pensions, and clinical lecturer in neurology, University of Oxford. 8°, cloth, 84 pp., with 20 illustrations. London: Edward Arnold and Company, 1952. $3.00. (Distributed by Williams and Wilkins, Baltimore.)

This small monograph reviews some of the aspects of the disease in the light of current knowledge. Dr. Russell points out that the various methods of handling paralyzed muscle can be subjected to simple physiologic tests. Much of the text is devoted to paralysis, its treatment and rehabilitation. There is a list of references and an index. As an expression of British opinion, the small book should be in all collections on the subject.

Modern Medicine Annual 1953: An annual volume containing the articles that appeared in the twenty-four issues of Modern Medicine during 1952. 12°, cloth, 1413 pp., with illustrations. Minneapolis: Modern Medicine, 1953. $6.00.

This new volume of a long series contains the articles published in the 24 numbers of *Modern Medicine* published in 1952. They have been rearranged according to classes, and author and subject indexes have been provided.

Klinische Fehldiagnosen. By Prof. Dr. M. Bürger, director, Med. Universitätsklinik, Leipzig. 8°, cloth, 481 pp., with 185 illustrations and 52 tables. Stuttgart: Georg Thieme, 1953. DM 58.50. (Distributed by Grune and Stratton, New York.)

This comprehensive treatise on errors in diagnosis covers the whole field of general medicine. The text ends with a table of false and correct diagnoses. There is a good index, and the publishing is excellent. This valuable contribution to diagnosis merits translation into English.

Clinical Diagnosis by Laboratory Methods: A working manual of clinical pathology. By James C. Todd, Ph.B., M.D.; Arthur H. Sanford, A.M., M.D., director of laboratories, Rochester State Hospital; and Benjamin B. Wells, M.D., Ph.D., professor of medicine, Department of Medicine, University of Arkansas School of Medicine. Twelfth edition. 8°, cloth, 998 pp., with 946 illustrations. Philadelphia: W. B. Saunders Company, 1953. $8.50.

This standard textbook was first published in 1908, and in this edition Dr. Wells has been added as a co-author. The text has been brought up to date. An appendix presents an index outline of laboratory findings in important diseases. There is a comprehensive index.

This Is Your Job. By the State of New York Department of Mental Hygiene. 12°, paper, 33 pp., with illustrations. New York: State of New York Department of Mental Hygiene, 1953. $0.20.

This manual has been prepared for the 28,000 persons employed in the 17 mental institutions of New York State. It is an easy-to-read guide to institutional service, and discusses employee relations and presents the regulations of the department.

Children of Divorce. By J. Louise Despert, M.D. 8°, cloth, 282 pp. Garden City, New York: Doubleday and Company, Incorporated, 1953. $3.50.

Dr. Despert, a child psychiatrist who has been associated with Cornell University for the past fifteen years, discusses the problem of how children may be helped to absorb the experience of divorce with the least amount of damage to their welfare.

The Yearbook of Psychoanalysis: Vol. 8 (1952). By Sandor Lorand, M.D. 8°, cloth, 383 pp. New York: International Universities Press, Incorporated, 1953. $7.50.

This new volume in an important series contains 24 articles on various topics in psychoanalysis.

Fundamentals of Clinical Cancer with Emphasis on Early Diagnosis and Treatment. By Leonard B. Goldman, M.D., clinical professor of radiotherapy, New York Medical College, Flower and Fifth Avenue Hospitals, chairman, Tumor Conference, and director, Radiation Therapy Department, Queens General Hospital, and consultant radiation therapist, Flushing, Rockaway Beach and Triboro hospitals, New York City. 4°, cloth, 312 pp., with 221 illustrations. New York: Grune and Stratton, 1953. $8.75.

Dr. Goldman stresses the importance of the early diagnosis and treatment of cancer and allied malignant growths. In the material on treatment, chemotherapy has been included because of the author's belief in its value as a remedial agent. The material is arranged by structures and regions. In order are discussed tumors of the skin, head and neck, chest, gastrointestinal tract, genitourinary tract, breast, gynecologic tract, and lymphoblastoma and leukemia, malignant tumors of childhood, sarcoma of soft tissues and tumors of bone. There is a good index, and the book is well published.

The Founders of Neurology: One hundred and thirty-three biographical sketches. By 84 authors. Edited by Webb Haymaker, M.D., chief, Neuropathology Section, Armed Forces Institute of Pathology, Washington, D. C. With the bibliographic and editorial assistance of Karl A. Baer, bibliographer, Army Medical Library, Washington, D. C. 8°, cloth, 479 pp., with photographs. Springfield, Illinois: Charles C Thomas, 1953. $10.50.

This composite book is based on material prepared by the Army Medical Library in 1949 to supplement an exhibition by the Armed Forces Institute of Pathology for the Fourth International Neurological Congress, held in Paris, in 1949. The text is divided into five parts: neuroanatomists, neurophysiologists, neuropathologists, clinical neurologists and neurosurgeons. The material consists of pictures and short biographic sketches of 133 eminent physicians and surgeons, written by 84 authors. There is a good index. The book should be in all collections on medical history and neurology.

Functional Disorders of the Foot: Diagnosis and treatment. By Frank D. Dickson, M.D., clinical professor of surgery, University of Kansas School of Medicine, orthopedic surgeon, St. Luke's, Kansas City General, and Wheatley hospitals, Kansas City, Missouri, and Providence Hospital, Kansas City, Kansas; and Rex L. Diveley, M.D., assistant professor of orthopedic surgery, University of Kansas School of Medicine, chief orthopedic consultant, Veterans Administration, Washington, D.C., chief orthopedic surgeon, Kansas City General Hospital, and orthopedic surgeon, St. Luke's and Wheatley hospitals, Kansas City, Missouri, and Providence Hospital, Kansas City, Kansas. Third edition. 8°, cloth, 345 pp., with 205 illustrations. Philadelphia: J. B. Lippincott Company, 1953. $6.75.

In this new edition of a special monograph first published in 1939 the authors have added material on architectural defects of bones as a cause of foot imbalance, the correction of flatfoot and hallux valgus, intractable plantar warts and deformity of the toe nails. The subject of rigid flatfoot has been rewritten, and the text has been revised in a number of places to include more detail for the sake of clarity. There is a good index, and the publishing is excellent.

Washing our Water: Your job and mine. By Helen B. Woodward. 12°, paper, 28 pp., with illustrations. New York: Public Affairs Pamphlets, 1953. $0.25. (Public Affairs Pamphlet No. 193.)

The author discusses pollution control and sewage treatment.

Hypersplenism and Surgery of the Spleen. By William Dameshek, M.D., and C. Stuart Welch, M.D., of the Pratt Diagnostic Hospital, New England Center Hospital and Tufts College Medical School, Boston. Based on exhibits presented at the annual meetings in 1947 and 1951 of the American Medical Association. Recipients in 1951 of the A.M.A. Silver Medal. 4°, paper, 84 pp., with illustrations. New York: Grune and Stratton, 1953. $10.00.

The material in this volume is presented in graphic form is an extension of the book by Dameshek and Estren, *Spleen and Hypersplenism*, published in 1948. It has much new material on hemolytic anemia and idiopathic thrombocytopenic purpura, with new sections on methods for splenectomy and the relief of portal hypertension.

Recurrent Dislocation of the Shoulder. By James A. Dickson, M.D., chief, Department of Orthopedic Surgery, Cleveland Clinic and Cleveland Clinic Hospital; Alfred W. Humphries, M.D., member, Department of Orthopedic Surgery, Cleveland Clinic and Cleveland Clinic Hospital; and Harry W. O'Dell, M.D., chief, Department of Orthopedic Surgery, Akron Clinic. 8°, cloth, 158 pp., with 78 illustrations. Baltimore: Williams and Wilkins, 1953. $4.50.

The authors in this small monograph discuss the embryology, anatomy and physiology of the shoulder, and the pathology and treatment of recurrent dislocation. The pertinent literature is surveyed, and a bibliography is appended to the text. There are indexes of authors and subjects. The book should be in collections on orthopedics.

From the Workshop of Discoveries. By Otto Loewi, research professor of pharmacology, New York University College of Medicine. 8°, cloth, 62 pp. Lawrence, Kansas: University of Kansas Press, 1953. $2.00. (*Porter Lectures*, Series 19.)

The author, in the lecture that features the title, discusses the manner in which discoveries are made. To this are added two lectures entitled "Reflections on the Study of Medicine" and "Problems in the Field of Adrenal Function," which consider the study and practice of medicine from a broad, philosophic point of view and present a synthesis of recent studies on adrenal function.

Sympathetic Control of Human Blood Vessels. By H. Barcroft, M.A., M.D., M.R.C.P., professor of physiology, St. Thomas's Hospital Medical School, London; and H. J. C. Swan, Ph.D., M.B., B.S., M.R.C.P, research associate, Mayo Clinic, Rochester, Minnesota. 8°, cloth, 165 pp., with illustrations. London: Edward Arnold and Company, 1953. $3.75. (Distributed by Williams and Wilkins, Baltimore.) (Monographs of the Physiological Society, No. 1.)

This monograph is based primarily on studies on the circulation in the extremities and on a survey of the literature. Lists of references are appended to the chapters and there are indexes of authors and subjects.

The Interpersonal Theory of Psychiatry. By Harry S. Sullivan, M.D. Edited by Helen S. Perry and Mary L. Gawel. With an introduction by Mabel B. Cohen, M.D. 8°, cloth, 393 pp. New York: W. W. Norton and Company, Incorporated, 1953. $5.00.

This book constitutes the unpublished lectures of Dr. Sullivan, who died in 1949. He gave 6 series of lectures at the Washington School of Psychiatry and the William Alanson White Institute of Psychiatry. The text is divided into three main parts: introductory concepts; developmental epochs; and patterns of inadequate or inappropriate interpersonal relations. There is a good index, and the book is well published. It should be in collections on psychiatry.

Diseases in Children. Edited by Alan Moncrieff, C.B.E., M.D., F.R.C.P., Nuffield Professor of Child Health, University of London, physician, Hospital for Sick Children, Great Ormond Street, and consulting physician, Children's Department, Middlesex Hospital; and Philip Evans, M.D., M.Sc., F.R.C.P., physician, to the Children's Department and director of the Department of Child Health, Guy's Hospital, and physician, Hospital

for Sick Children, Great Ormond Street Fifth edition. 8°, cloth. Two volumes. Vol. 1, 1014 pp., with 323 illustrations; Vol. 2, 959 pp., with 367 illustrations. London: Edward Arnold and Company, 1953. $21.00 for the set. (Distributed by Williams and Wilkins, Baltimore.)

The first edition of this treatise was published in 1913. This new edition is the joint work of 50 contributors. The text has been revised and brought up to date, including new material on the causes of congenital malformations, growth and development, kwashiorkor, endocrine disorders, disorders of the teeth and jaws, the alimentary tract and congenital heart disease. Lists of references refer to the various subjects. The two volumes are paged consecutively, and there is a good index. The publishing is excellent. The work should be in all collections on pediatrics.

Operative Gynecology. By Richard W. TeLinde, M.D., professor of gynecology, Johns Hopkins University School of Medicine, and chief gynecologist, Johns Hopkins Hospital. Second edition. 4°, cloth, 902 pp., with 409 illustrations and 7 color plates. Philadelphia: J. B. Lippincott Company, 1953. $20.00.

In this new edition of a book first published in 1946 the text has been thoroughly revised and chapters on the use of pessaries, the surgery of the double uterus, culdoscopy, carcinoma of the cervix in situ and sarcoma of the uterus have been added. Lists of references are appended to the chapters. There is an extensive index, and the publishing is excellent.

The Conception of Disease: Its history, its versions and its nature. By Walther Riese, M.D., on the staff of the following institutions: Medical College of Virginia, Department of Mental Hygiene and Hospitals of the Commonwealth of Virginia, Richmond Professional Institute, College of William and Mary and Washington School of Psychiatry. 8°, cloth, 120 pp. New York: Philosophical Library, 1953. $3.75.

The author discusses the conception of disease from its anthropologic and moral implications. There are special chapters on the relation between art and disease, and Leonardo da Vinci's contributions to the genesis of the anatomic conception of disease. The author was previously associated with the medical faculties of Frankfurt am Main, Lyons and the Sorbonne in Paris.

Textbook of Public Health: (Formerly Hope and Stallybrass). By W. M. Frazer, O.B.E., M.D., Ch.B., M.Sc., D.P.H., barrister-at-law, Gray's Inn, medical officer of health, City and Port of Liverpool, and medical officer to the Liverpool Education Committee, and professor of public health, University of Liverpool. Thirteenth edition. 8°, cloth, 663 pp., with 76 illustrations and 43 tables. London: E. & S. Livingstone, Ltd., 1953. $8.50. (Distributed by Williams and Wilkins, Baltimore.)

This standard British book has been thoroughly revised and brought up to date in accordance with the changes in the Public Health and Hospital Services of England. A new chapter describes in detail the National Health Service and the functions of the new statutory bodies arising from it. The effect of the Act upon the Mental Health Service, maternity and child welfare and the services dealing with tuberculosis and venereal diseases are considered in their proper places in the text. The National Assistance Act, which primarily had the effect of abolishing the Poor Law, is described. The chapter on the supervision of milk supplies has been entirely rewritten in accordance with parliamentary legislation. The material covers the ground required for the diploma in public health under the General Medical Council's postwar rules. There is an extensive index. The book is well published and should be in all collections on public health.

Diseases of the Digestive System. Edited by Sidney A. Portis, M.D., associate clinical professor of medicine, University of Illinois College of Medicine, senior attending physician, Department of Medicine, Michael Reese Hospital, consulting physician, Cook County Hospital, and chief of the medical services of the Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital, Chicago. Third edition. 4°, cloth, 1119 pp., with 274 illustrations. Philadelphia: Lea and Febiger, 1953. $20.00.

This new edition of a standard work, written by 57 physicians, has been thoroughly revised and brought up to date. The physiology of the gastrointestinal tract has been treated thoroughly as a groundwork for the clinical manifestations of disease. Lists of references are appended to the chapters, and there is a good index. The publishing is excellent. The book should be in all collections on the subject.

Adjustment to Physical Handicap and Illness: A survey of the social psychology of physique and disability. By Roger G. Barker. With the collaboration of Beatrice A. Wright, Lee Meyerson and Mollie R. Gonick. Second edition revised 8°, paper, 440 pp., with illustrations. New York: Social Science Research Council, 1953 $2.00. (Bulletin No. 55, revised.)

The second edition of this bulletin, first published in 1946, has been revised to include recent advances. A comprehensive bibliography of 48 pages, arranged by chapters, is appended to the text, and there are indexes of authors and subjects. The price is extremely low. The book is recommended for all medical libraries as a reference work and to all social workers and other interested persons.

NONCLINICAL NOTES

BULL OR HEIFER?

"Calf Girth Measurement a Valuable Diagnostic Aid." — News Release from The American Medical Association — Farm journals please copy.

GRANTS BY MASSACHUSETTS HEART ASSOCIATION

At a meeting of the Executive Committee of the Massachusetts Heart Association on September 29, 1953, the following grants, as recommended by the Research Allocations Committee were approved:

No. 79. Boston City Hospital: Studies of anticoagulants in cardiovascular disease, by Herbert S. Sise, M.D. — $2,200.00

No. 81. Massachusetts General Hospital: Continuation of studies on cardiorenal disease, by Alexander A. Leaf, M.D. — $4,108.00

No. 83. Boston University College of Liberal Arts: Circulation in the hamster cheek pouch as related to electrolyte imbalance, by George P. Fulton, Ph.D. — $3,567.75

No. 84. The Children's Hospital: The peripheral circulation of patients with congenital heart disease, especially the morphology, patho-physiology and etiology of the syndrome of "red fingers," by Alexander S. Nadas, M.D. — $3,780.00

No. 86. Boston University School of Medicine: Further studies of agents which decrease cardiac irritability and automaticity, by Chester W. White, M.D. — $2,530.00

No. 88. Beth Israel Hospital: Psychological aspects of operations on the heart, by Myron G. Sandifer, M.D., under the direction of Grete Bibring, M.D. — $2,045.00

It was further voted that the Association pledge itself to the amount of $10,000 for the Boston Medical Library, payable over a period of three years and collected from voluntary gifts from the thirteen chapters and the state organization, according to fair-share recommendations and that the sum of $2,000 be made available to the Postgraduate Medical Institute, charged to physician education.

NOTICES

ANNOUNCEMENT

Dr. S. N. Mangano announces the removal of his office to 51 Brattle Street, Cambridge, for the practice of general surgery.

BOSTON CITY HOSPITAL HOUSE OFFICERS' ASSOCIATION

The following lectures have been scheduled by the Boston City Hospital House Officers' Association, and will be held in the New Cheever Amphitheater, Dowling Building, Boston City Hospital, at 7 p.m. on the dates indicated:

Tuesday, November 17. Myxedema. Dr. George T. Harrell, Bowman Gray School of Medicine.

Monday, November 23 (tentative). To be announced. Dr. Maxwell Wintrobe, University of Utah.

Tuesday, December 1. Advances in Field of Poliomyelitis Research. Dr. Thomas Weller, Harvard School of Public Health.

Tuesday, December 8. Apical Localization of Pulmonary Tuberculosis. Dr. William Dock, State of New York Medical School at New York City.

Tuesday, December 15. Metabolism of Gout. Dr. De Witt Stetten, Jr., Public Health Research Institute, New York City.

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

The next meeting of the Middlesex South District Medical Society will be held at the Newton-Wellesley Hospital, Wednesday, November 18, at 8 p.m. Dr. John G. Downing, professor of dermatology, emeritus, Boston University School of Medicine and Tufts College Medical School, will speak on the subject "Mucosal and Cutaneous Clues in Medicine and Surgery." The discussers will be Drs. Bernard Appel and C. Guy Lane.

PROCTOLOGIC RESEARCH FELLOWSHIP

The International Academy of Proctology announces the establishment and award of a one-year Proctologic Research Fellowship in the amount of $1200.00. This grant has been awarded to the Jersey City Medical Center, New Jersey, to be administered under the direction of Dr. Earl J. Halligan, Surgical Director of the Medical Center.

Dr. Halligan is a former International President of the Academy. The Board of Trustees of the International Academy of Proctology will vote another fellowship grant of a similar amount at the time of the next annual meeting of the Academy. Thus, there will be at least two research fellowship studies in progress, in different institutions, under the auspices of the International Academy of Proctology.

PAN-AMERICAN ACADEMY OF GENERAL PRACTICE

The annual congress of the Pan-American Academy of General Practice will be held in Medellin, Colombia, February 15 to 20, 1954. The congress will be divided into sections representing medicine, surgery and pharmacy. After the meeting, a tour has been arranged to visit Bogota, Barranquilla and Montega Bay. Further information may be obtained from Dr. Arturo Martinez, Secretary, 500 West End Avenue, New York City.

SOCIETY MEETINGS AND CONFERENCES

November 6 and 7. American College of Cardiology. Page 506, issue of September 17.

November 7 and 21. Symposium on Industrial Nursing. Page 714, issue of October 22.

November 9. Fried Lecture. Page 634, issue of October 8.

November 9–11. Association of Military Surgeons. Page 750, issue of October 29.

November 9–13. American Public Health Association. Annual Meeting. Page 750, issue of October 29.

November 9–25. Consultation Clinics for Crippled Children. Page 713, issue of October 22.

November 9, 11, 13, 17 and 19. Warren Prize Lectures. Page 750, issue of October 29.

November 10–December 15. Boston City Hospital House Officers' Association Lectures. Page 789.

November 11–December 2. Course in Child Psychiatry (Pediatric neuropsychiatry). Page 428, issue of September 3.

November 12–14. Annual Convention of the National Society for Crippled Children and Adults. Chicago.

November 16 and 17. New England Diabetes Fair. Horticultural Hall. Page 750, issue of October 29.

November 16–December 21. Hartford Medical Society Program. Page 260, issue of August 6.

November 18. Massachusetts Society of Examining Physicians. Page 546, issue of September 24.

November 18. Middlesex South District Medical Society. Notice above.

November 19 and 20. Inter-Society Cytology Council. Page 170, issue of July 23.

November 20–December 18. Boston Lying-in Hospital Journal Club. Page 672, issue of October 15.

December 6. American Academy of Dental Medicine. Page 170, issue of July 23.

January 6, March 3 and April 21, 1954. Massachusetts Society for Research in Psychiatry. Page 750, issue of October 29.

February 2–4. Examination for Public Health Service Medical Officers. Page 750, issue of October 29.

February 15–20. Pan-American Academy of General Practice. Notice above.

May 31–June 3. American Urological Association. Page xvii, issue of July 23.

September 12–15. Second International Congress of Cardiology. Page 44, issue of July 2.

September 16–18. American Heart Association. Annual Scientific Sessions. Page 44, issue of July 2.

District Medical Societies

MIDDLESEX EAST

November 18.

January 20. (Combined with the Auxiliary.)

March 24.

May 12. Annual Meeting. (Harlow Dinner.)

MIDDLESEX SOUTH

November 18.

Calendar of Boston District for the Week Beginning Thursday, November 12

THURSDAY, NOVEMBER 12

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.

*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.

*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.

*4:30–5:30 p.m. Diagnosis and Treatment of Diseases of Small Bowel. Dr. J. McGirr. Nurses' Home, Cambridge City Hospital.

*5:00 p.m. Case Presentation and Pathological Discussion Followed by a Subject of Special Presentation. Joslin Amphitheater, New England Deaconess Hospital.

*5:00–6:00 p.m. Surgical Division Meeting. Mount Auburn Hospital, Cambridge.

FRIDAY, NOVEMBER 13

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.

*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

*12:30–1:30 p.m. Medical Diseases Simulating Acute Abdomen. Dr. E. Hinton. Ward B Classroom, Cambridge City Hospital.

*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.

*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.

*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.

*4:30 p.m. Warren Prize Lecture. Biochemical Aspects of Infections. Dr. René J. Dubos. Morse Auditorium, Museum of Science.

SATURDAY, NOVEMBER 14

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*9:00 a.m. Proctology Clinic. Peter Bent Brigham Hospital.

*9:00 a.m. Alcoholism Clinic. Peter Bent Brigham Hospital.

10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

11:00 a.m.–12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, NOVEMBER 16

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Foot Problems. New England Deaconess Hospital.

*8:30–9:30 a.m. Clinic by entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building, Boston City Hospital.

(Notices concluded on page six)